Imperial College London

The Prevalence of Abdominal Aortic Aneurysm (AAA): an Ultrasound Screening program for the aging population in multicentre across Riyadh

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This thesis is submitted in fulfilment of the requirements of the degree of Doctor of Philosophy (PhD)

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Abstract

Introduction: Abdominal aortic aneurysm (AAA) is characterized by permanent dilatation of the aortic wall. If it ruptures, fatality rates might exceed 80%. Screening elderly men for AAA is cost-effective and decreases mortality rates in Western nations. In Saudi Arabia, little research has been conducted. Establishing a screening program might lower AAA rupture mortality risk. Because of their lower cost, and compact size, handheld ultrasound devices may be suitable for mass screening. Shear wave elastography (SWE) has emerged as a tool for assessing the elastic properties of the aortic wall, improving AAA diagnosis.

Hypothesis: This research aimed to determine AAA prevalence in the elderly population of Riyadh city and investigate associated risk factors, examine elastic properties of aneurysmal aortic walls using SWE, and assess the reliability of the Butterfly iQ probe as a diagnostic tool.

Methods: Three prospective analytic investigations were carried out. The first study screened individuals (n=680) for AAA across multiple hospitals in Riyadh. The second research utilized SWE ultrasound to evaluate participants' aortas. In the last study, two operators scanned AAA patients using conventional and Butterfly probes.

Results: The study revealed a prevalence of 1% (95% CI 0.4% - 2.1%) and a high association between AAA and male gender and smoking, a significant difference in wall stiffness between AAA cases and controls **(p <0.001)**, and Intra- and inter-operator interclass correlation coefficient (ICC) values greater than 0.9, indicating excellent agreement. The Bland-Altman limits of agreement were similar for both methods.

Conclusion: The prevalence of AAA in Riyadh is trending similarly to Western nations. National screening for AAA should be considered and investigated. Advances in ultrasound technologies have increased surveillance capabilities, and changes in aortic wall elasticity may be early warning signs. The Butterfly iQ probe is effective in detecting AAA, potentially replacing conventional ultrasound machines in community mass screenings.

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Statement of Originality

I hereby certify that the research presented in this thesis is original and that it has not been previously submitted for any other academic degree or qualification nor utilized for any other purpose.

Part of the data from this study has been submitted as an abstract to the Vascular Society for presentation at their annual conference in November 2023.

Declaration of the candidate

I declare that this work has been conducted solely by myself within Imperial College London and does not overlap with any other institutes ore departments, I confirm that the thesis adheres to the principles of academic integrity and has been produced in accordance with the guidelines and regulations of Imperial College London. To the best of my knowledge and belief, the thesis does not infringe upon copyright of any individual or entity and does not contain any material that has been previously published, unless appropriately referenced.

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Dedication

I would like to dedicate my work to my beloved parents, Saad and Wafa, who have always been my role models and a constant source of encouragement throughout my academic pursuit. Their love, support, and sacrifices have been essential for my success, and I am eternally grateful for them.

I also dedicate this work to my wonderful husband, Waddah, for his constant support and company during my academic journey. I could not have done it without his support and patience.

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List of abbreviations

AAA	Abdominal Aortic Aneurysm
CAD	Coronary Artery disease
CASS	Collaborative Aneurysm Screening Group
CTA	Computed Tomography Angiography
CVD	Cardiovascular Disease
ECM	Extracellular Matrix
ECG	Electrocardiogram
EVAR	Endovascular Aortic Repair
ICC	Interclass Correlation Coefficient
ICER	Incremental Cost Effectiveness Ratio
ITI	Inner to Inner
KAAUH	King Abdullah bin Abdul-Aziz University Hospital
KAIMRC	King Abdullah International Medical Research Centre
KKUH	King Khalid University Hospital
KSMC	King Saud Medical City
LELE	Leading Edge to Leading Edge
MASS	Multicentre Aneurysm Screening Study
MMP	Matrix Metalloproteinases
NAAASP	National Abdominal Aneurysm Screening Program
NGHA	National Guard Health Affairs
NICE	National Institute for Health and Care Excellence
OSR	Open Surgical Repair

OTO	Outer to Outer
PACS	Picture Archiving Communication System
PAD	Peripheral Arterial Disease
PNU	Princess Norah University
QALY	Quality-Adjusted Life Year
REDCap	Research Electronic Data Capture
RDS	Research Design Service
SMCs	Smooth Muscle Cells
SWE	Shear Wave Elastography
TTE	Transthoracic Echocardiography
UKSAT	UK Small Aneurysm Trial
USPSTF	U.S Preventive Service Task Force

CHAPTER 1: Introduction

1.1 Background

Cardiovascular disease, Peripheral arterial disease, and Aortic aneurysms have distinct clinical presentations and therapeutic techniques; however, they are linked by the underlying pathophysiological mechanisms involving atherosclerosis. understanding the scientific link between these illnesses is critical for risk assessment, prevention, and management of disease.

1.1.1Cardio-vascular disease

Cardiovascular disease (CVD) is a critical global health issue; it is considered the leading cause of death in the world, accounting for around 17.9 million deaths per year (WHO, 2021). CVD refers to a group of heart and blood vessel diseases such as coronary artery disease, heart failure, and stroke. Many studies have been undertaken to investigate the epidemiology, pathogenesis, and management of CVD. It has been shown to have a complex pathophysiology and a variety of risk factors, including hypertension, diabetes, obesity, smoking, and a family history of CVD (Chahine, 2022). CVD etiology is characterized by a complex combination of genetic, environmental, and behavioral factors, resulting in atherosclerosis and plaque formation inside the arterial walls. Decreased blood flow to the heart and other vital organs can result in a variety of symptoms and complications. Its prevention and management require a comprehensive approach that involves both lifestyle changes and pharmaceutical therapies. Early detection and management of CVD risk factors are essential for reducing its burden (Brunström & Carlberg, 2018; Kaptoge, Sundström & Di Angelantonio, 2019).

1.1.2 Peripheral artery disease

Peripheral artery disease (PAD) is a common illness affecting roughly 200 million individuals globally (Fowkes et al., 2013). It occurs as a result of arteries supplying blood to the legs and feet becoming narrowed or clogged secondary to plaque accumulation (atherosclerosis) (Figure 1.1).

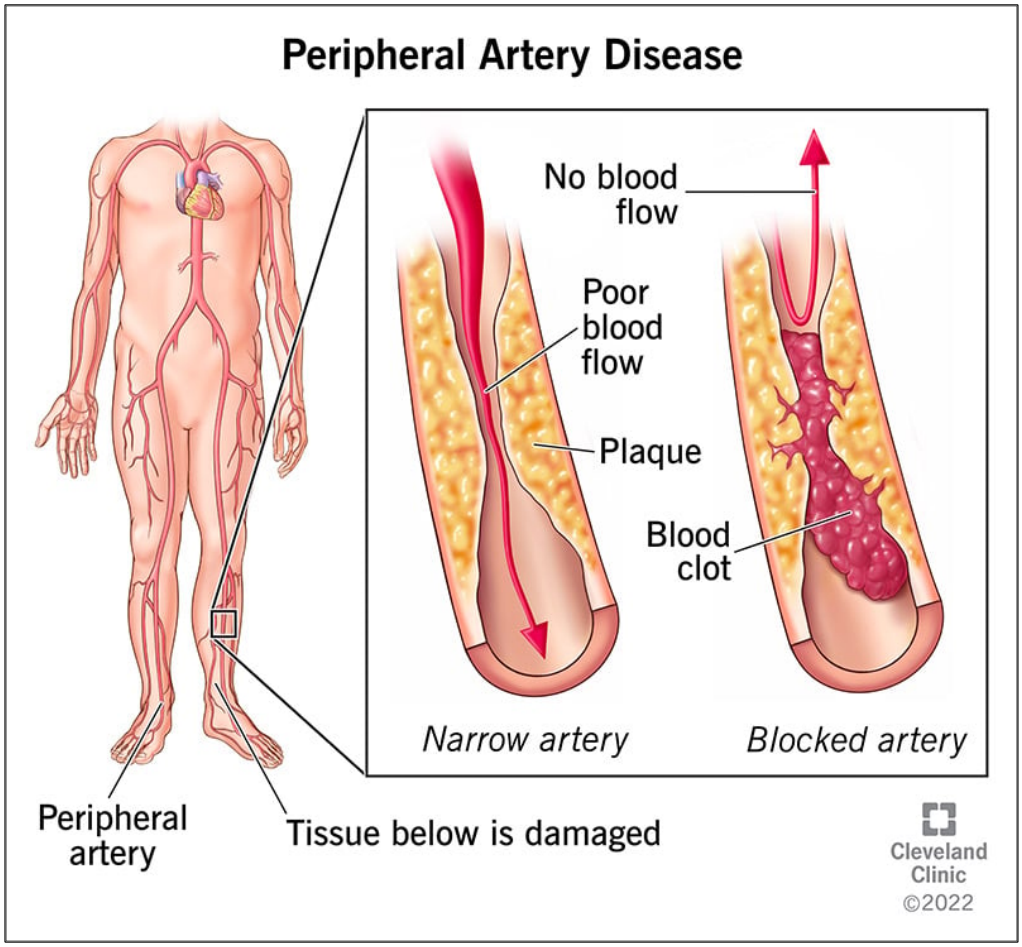


Figure 1. 1 *Narrowed and blocked arteries in PAD.* *(Cleveland clinic,2022)*

As a result of decreased blood flow and oxygen supply to the affected areas, symptoms such as leg discomfort, cramps, and weakness may occur (Figure 1.2). Smoking, diabetes, high blood pressure, high cholesterol levels, family history, and sedentary lifestyle are

acknowledged risk factors for PAD. Early detection and management of PAD are essential for preventing disease development and decreasing the likelihood of consequences such as amputation (Gerhard-Herman et al., 2017).

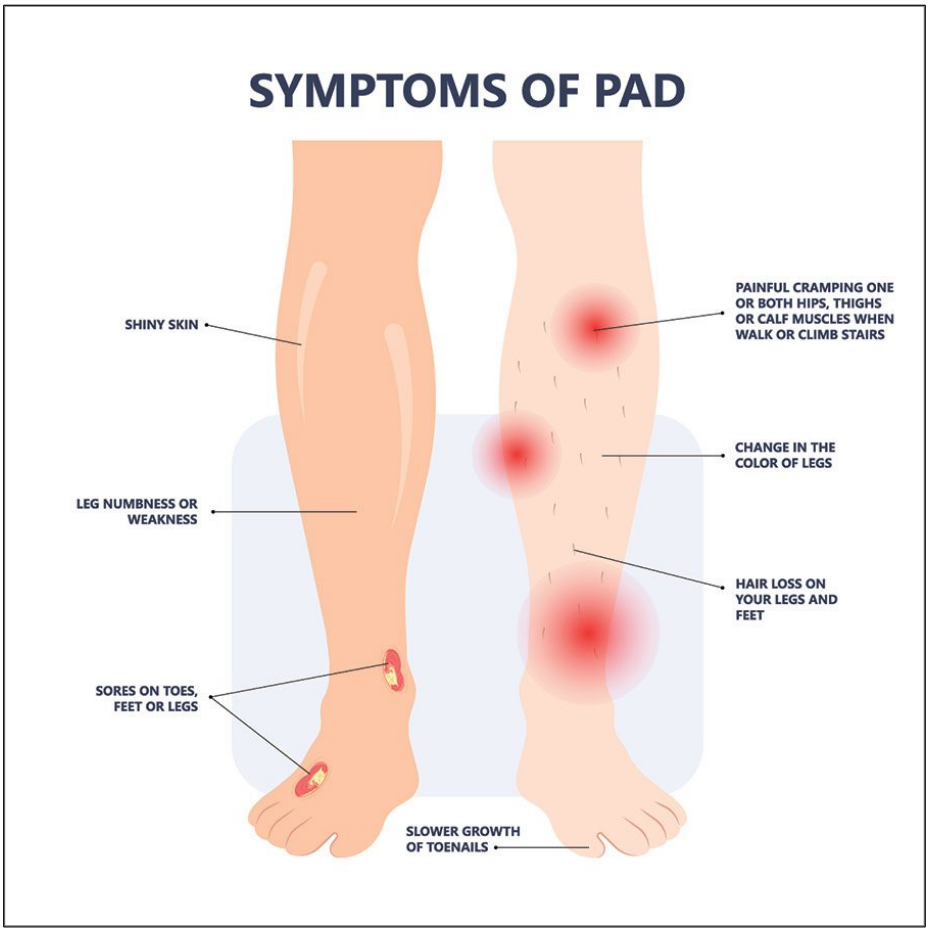


Figure 1. 2 *Peripheral arterial disease symptoms.* *(Fairfax Vascular Center, 2023)*

1.1.3 Aortic Aneurysm

The term aneurysm is derived from the Greek word "ανευρυσμμα " - aneurusma - which means "a widening." An aneurysm is often described as a localized irreversible dilatation of an artery with a diameter greater than 3 cm (Figures 1.3 & 1.4). Others have attempted to define AAA

as the maximal infrarenal aortic diameter being 1.5 times the predicted normal diameter to adjust for individual variation (Lederle, F. A. et al., 1997) (Moll et al., 2011) .

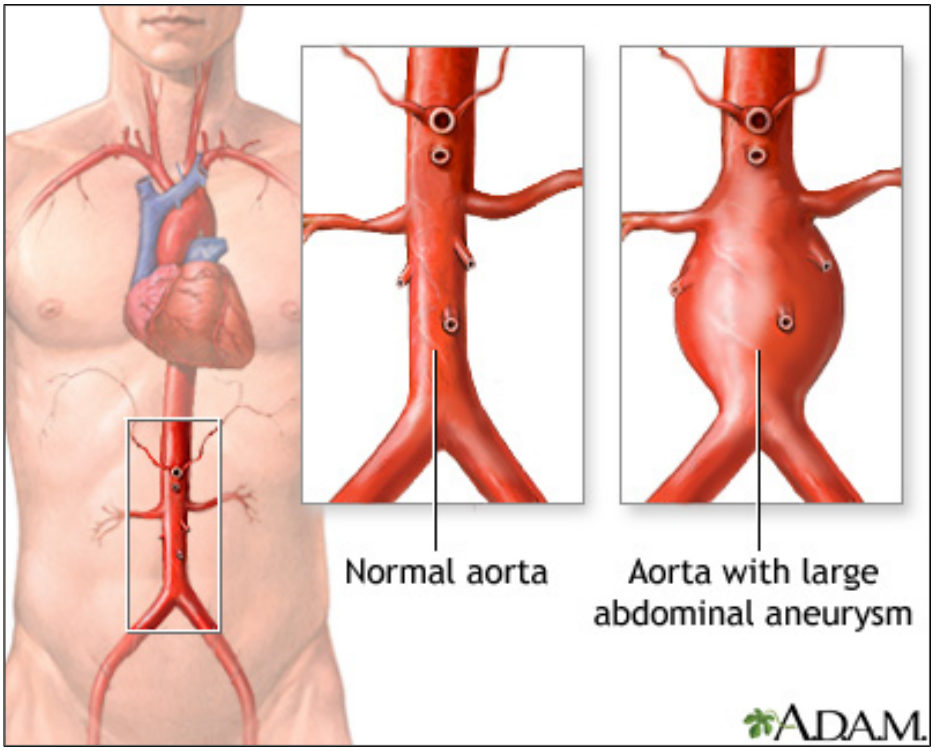


Figure 1. 3 *Infrarenal Abdominal Aortic Aneurysm (AAA).* *(A.D.A.M.,)*

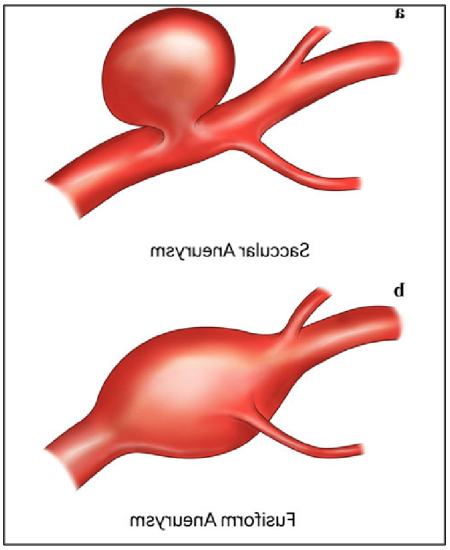


Figure 1. 4 *Aneurysm shapes.* *(Withers, Carolan-Rees & Dale, 2013)*

An abdominal aortic aneurysm (AAA) is categorized based on its location relative to the renal arteries as juxtrarenal, suprarenal, or infrarenal based on its location (Figure1.5)Infrarenal is the most common location of AAA, accounting for around 80-90% of all AAAs.Other typical places for aneurysms are the iliac, femoral, and popliteal arteries, and if an individual has an aneurysm in one location, he or she commonly has one in another. For example, 85% of people with a femoral artery aneurysm have a AAA, and 62% have a popliteal artery aneurysm (Moll et al., 2011). 14% of males with AAA have a femoral or popliteal artery aneurysm (Diwan et al., 2000). AAA rupture occurs when the aortic wall stress exceeds the aortic wall's mechanical strength (Haller et al., 2018) .

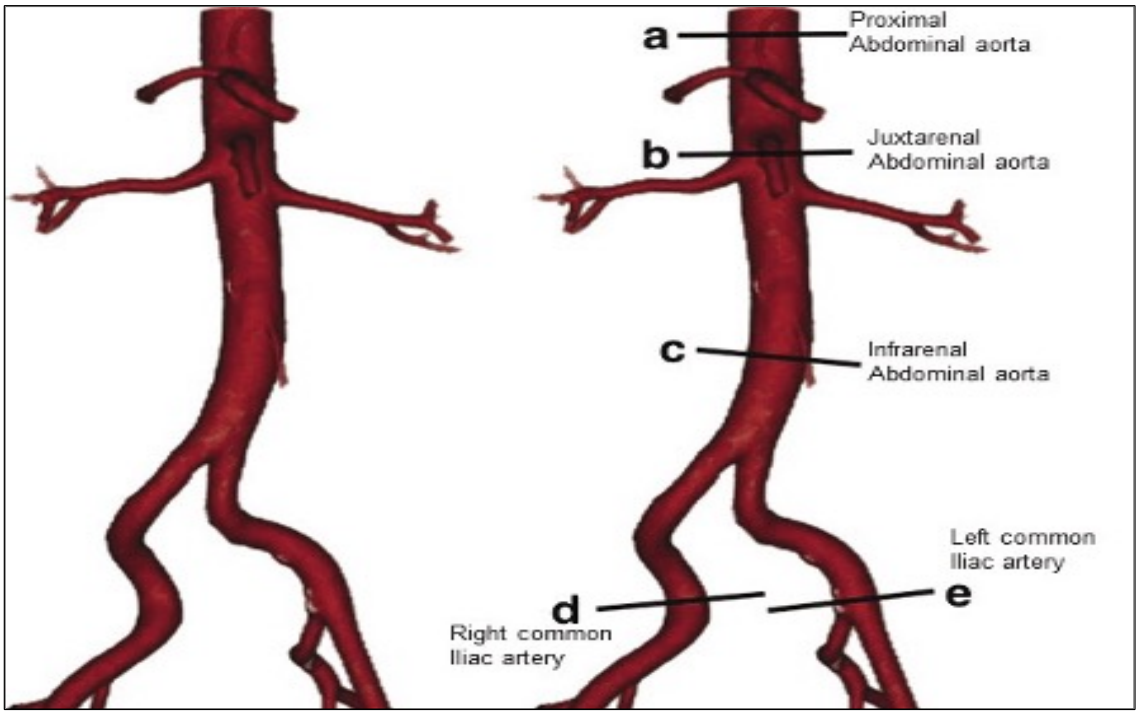


Figure 1. 5 *volume rendered image of the normal aorta indicating possible sites of aneurysms.* *(Sauceda, 2021)*

1.2 Anatomy

The aorta is the largest high-pressure artery and the primary blood supply, and it is divided into four segments: the ascending aorta, the aortic arch, the descending thoracic aorta, and the abdominal aorta (Figure 1.6).

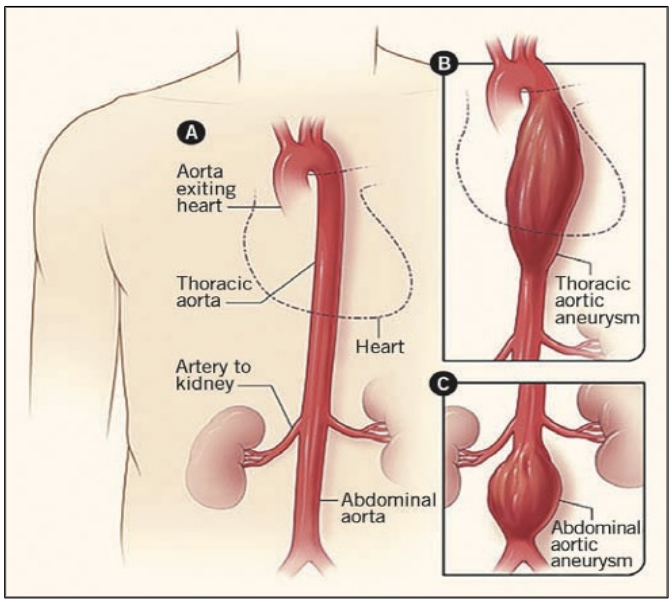


Figure 1. 6 *A) Anatomy of the aorta, B), & C) Aortic aneurysms.* *(Howell & Rabener, 2016)*

The abdominal aorta starts at the diaphragm and passes anteriorly to the spine in the retroperitoneal area before dividing into the left and right iliac arteries at the umbilicus. The artery wall is thick and composed of many layers known as the intima, media, and adventitia. The media, or middle layer, composed of elastin, collagen, and proteoglycans around one layer of smooth muscle, determines the vessel's strength, structure, and elasticity (Figure 1.7 &1.8). Aortic atherosclerosis, abdominal aortic aneurysm (AAA), aortic stenosis, aortic regurgitation, and aortic dissection are all pathologies involving the aorta (Howell & Rabener, 2016).

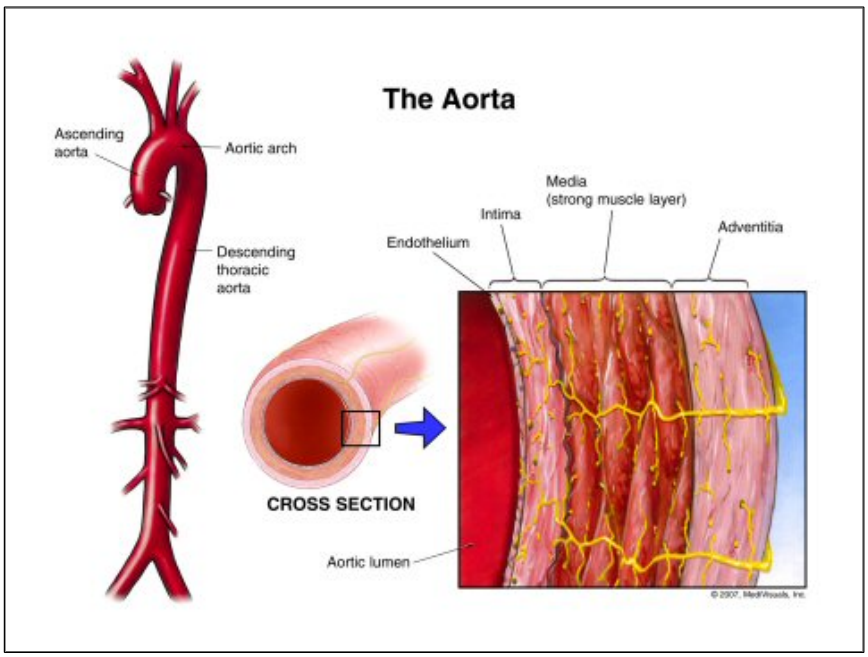


Figure 1. *7 Layers of aortic wall.* *(VCUhealth, 2023)*

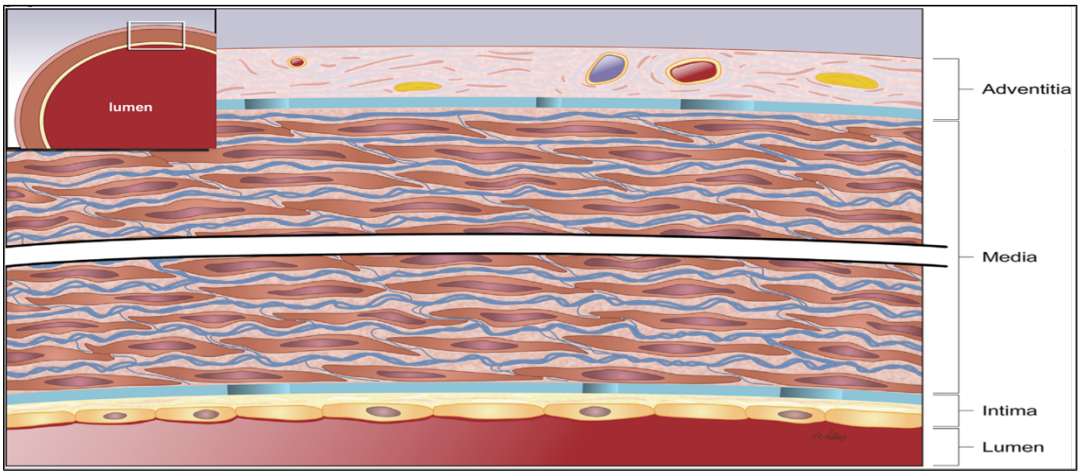


Figure 1. 8 *Aortic wall structure.* *(Shen, Ying H.,M.D., PhD. & LeMaire, 2017)*

1.3 Epidemiology

Abdominal aortic aneurysm (AAA) is a serious vascular disease with unique epidemiology. AAAs are completely asymptomatic until they rupture, resulting in mortality in 65% of patients (outside-of-hospital deaths plus perioperative mortality) (Sakalihasan, Limet & Defawe, 2005; van Beek et al., 2014). AAA occurrence increases as one ages and is more prevalent in men

than women (Sweeting et al., 2018). Smoking is the most significant risk factor for AAA development, with a dose-dependent relationship between smoking intensity and aneurysm occurrence (Howard et al., 2015) (Altobelli et al., 2018); smoking is associated with a 3 to 4-fold risk of AAA development (Sprynger et al., 2019).Other risk factors include a family history of AAA, hypertension, and atherosclerosis (Alcorn et al., 1996) According to epidemiological research, Western nations screening programs reported a prevalence of AAA in males over the age of 65 ranging from 1.18 % to 4.9%, whereas it is lower in women (0.15%) (Chabok et al., 2016) (Carino et al., 2018). Over the past two decades, the prevalence of AAA was 0.92% globally in 2019 with the western Pacific region having the highest prevalence (1.3%) and the African region exhibiting the lowest prevalence (0.33%) (Song et al., 2023). AAA-related mortality has decreased in recent years, owing primarily to improvements in screening programs and elective repair. Screening programs reduced the risk of rupture by 38% and AAA-related death by 42% (Ali et al., 2016). Even so, the growth rate of AAA is remains similar (Oliver-Williams et al., 2018). ruptured AAA is still a substantial cause of death in males aged 65 to 85 years, accounting for around 1-2% of all deaths in Western nations (Carino et al., 2018). AAA epidemiology gives critical insights into the population's demographic distribution and risk variables, enabling the establishment of preventative initiatives, screening programs, and suitable therapeutic approaches.

1.4 Etiology

Traditionally, aortic aneurysm (AA) was believed to be a consequence of Atherosclerotic disease (Blanchard, Armenian & Friesen, 2000). Further research revealed that AA has a complicated etiology that involves a complex interaction of genetic predisposition and environmental factors. Chronic inflammation, which destroys extracellular matrix components within the artery wall, is a significant factor in AA formation. The imbalance between matrix

metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) causes gradual degradation of elastin and collagen fibers in the aortic wall. Some gene variants have been linked to an increased vulnerability to AA; hence, genetic factors play a crucial role (Sakalihasan, Limet & Defawe, 2005). Furthermore, risk factors such as advanced age, male gender, smoking, hypertension, atherosclerosis, and a family history of AA all contribute to the disease's development. Hemodynamic stress, such as elevated blood pressure, can also damage the artery wall, making people more prone to AAA formation (Bararu Bojan Bararu et al., 2023). Finally, the etiology of abdominal aortic aneurysm is a complicated combination of genetic, environmental, and physiological variables that culminate in structural degeneration of the aortic wall (Figure 1.9), leading to potentially life-threatening abdominal aortic dilatation and rupture. Understanding the underlying mechanisms of AA assists in identifying at-risk individuals, implementing preventive measures, and establishing targeted treatment strategies as no pharmaceutical therapy prevents its onset or progression (Robertson & Bown, 2018).

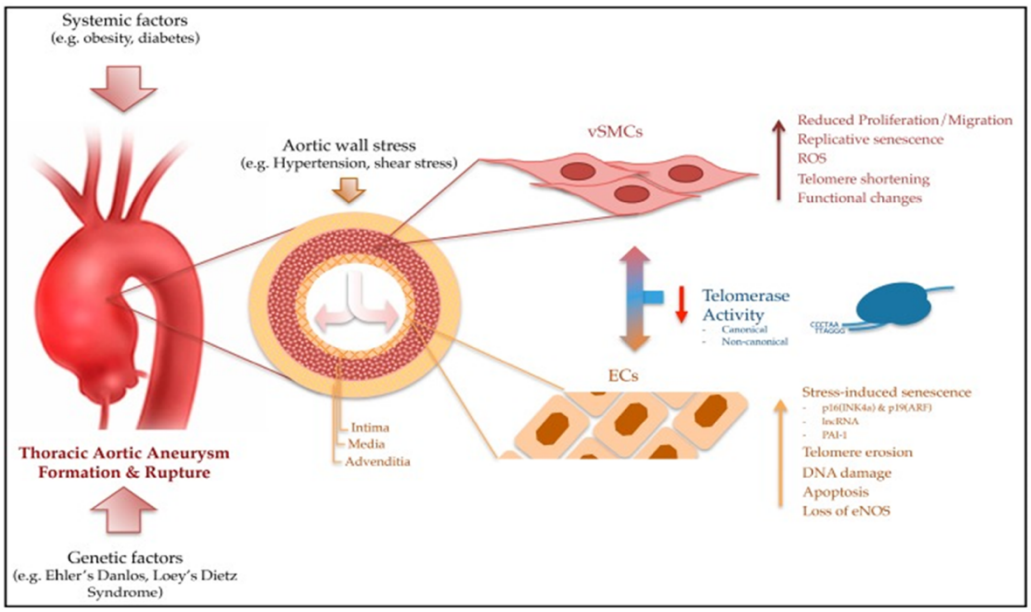


Figure 1. 9 *Mechanism of aneurysm development.* *(Bararu Bojan Bararu et al., 2023)*

1.5 Pathophysiology

The aorta wall is highly flexible, performing complicated biomechanical functions to ensure optimal flexibility and sufficient strength in response to changes in blood flow. Early changes in the development of arterial disease involve the accumulation of lipid deposits, inflammatory responses, and oxidative stress within the vessel wall. These, in turn, lead to a variety of pathological mechanisms that have been identified as potential contributors to the development of abdominal aortic aneurysms, dissections, and ruptures. Alteration and degradation of the aorta wall's cellular and extracellular components result in the gradual loss of smooth muscle cells (SMCs), destruction and loss of elastic fibers in the extracellular matrix (ECM), and aortic inflammation (Shen, Ying H.,M.D., PhD. & LeMaire, 2017). The formation of abdominal aortic aneurysms is closely linked to changes in the aortic wall's connective tissue, specifically the elastic fibers and fibrillar collagens, which have a substantial influence on the mechanical characteristics of the aorta. These changes in elastin and collagen observed within the aorta wall are dependent on the synthesis of proteases by resident vascular wall cells and matrix degradation caused by vascular inflammation, which is a significant pathophysiological mechanism (Figure 1.10). Additionally, most individuals with abdominal aortic aneurysms have a mural thrombus, which distinguishes it from arterial occlusive disorders. Unlike occlusive diseases, blood flow within aortic aneurysms is maintained, resulting in ongoing remodeling of the thrombus components (Sakalihasan, Limet & Defawe, 2005).

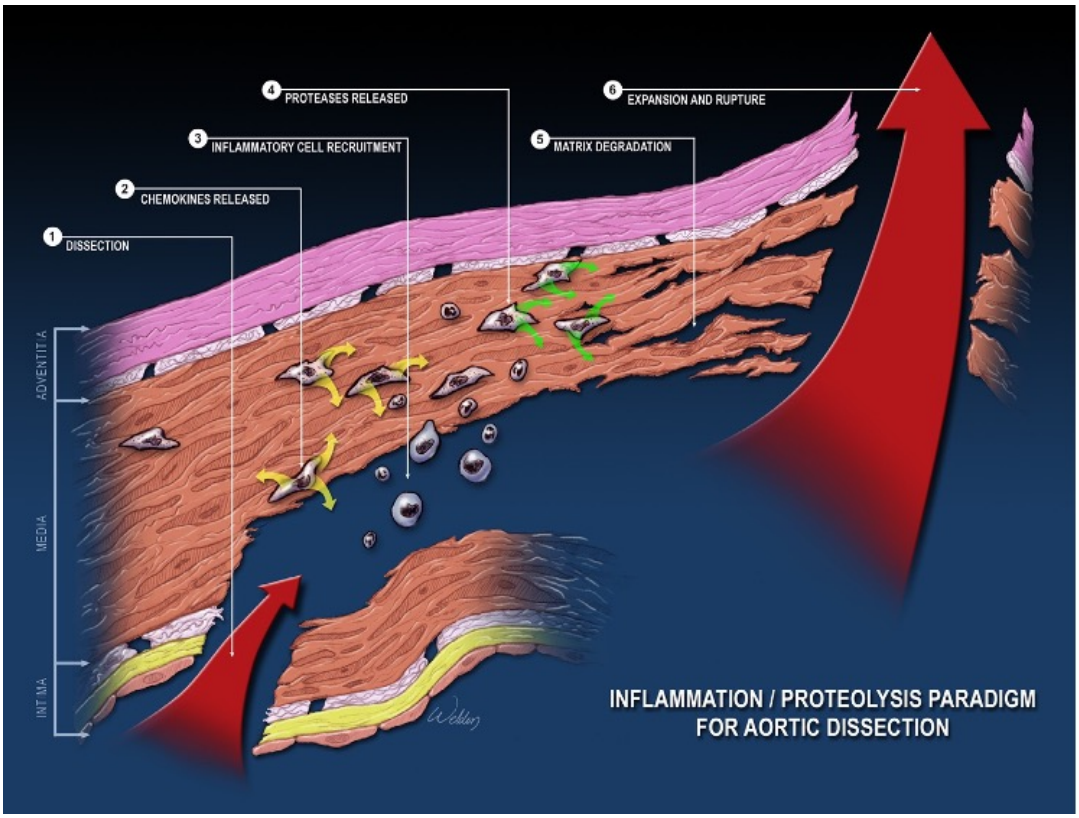


Figure 1. 10 *Aortic wall pathologic changes in AAA.* *(Shen, Ying H.,M.D., PhD. & LeMaire, 2017)*

1.6 Imaging techniques

1.6.1 Computed tomography (CT)

Computed tomography (CT) is the gold standard for operation planning and post-repair surveillance (Figure 1.11), it is recommended as was for diagnosis of AAA rupture, but it is not advised for screening owing to the use of contrast agents and exposure to ionizing radiation. CT scans, despite their elevated cost, enable for fast examination of the whole aorta. however, axial scans may not accurately show the actual aneurysm diameter due to aortic angulation within the body. (Kostun & Malik, 2016) CT scans are the gold standard for comparing results with other modalities such as ultrasound. It is important to remember, however, that CT takes

the maximum aorta diameter possible, whereas ultrasound measures perpendicular to the aortic lumen (Borgbjerg et al., 2018).

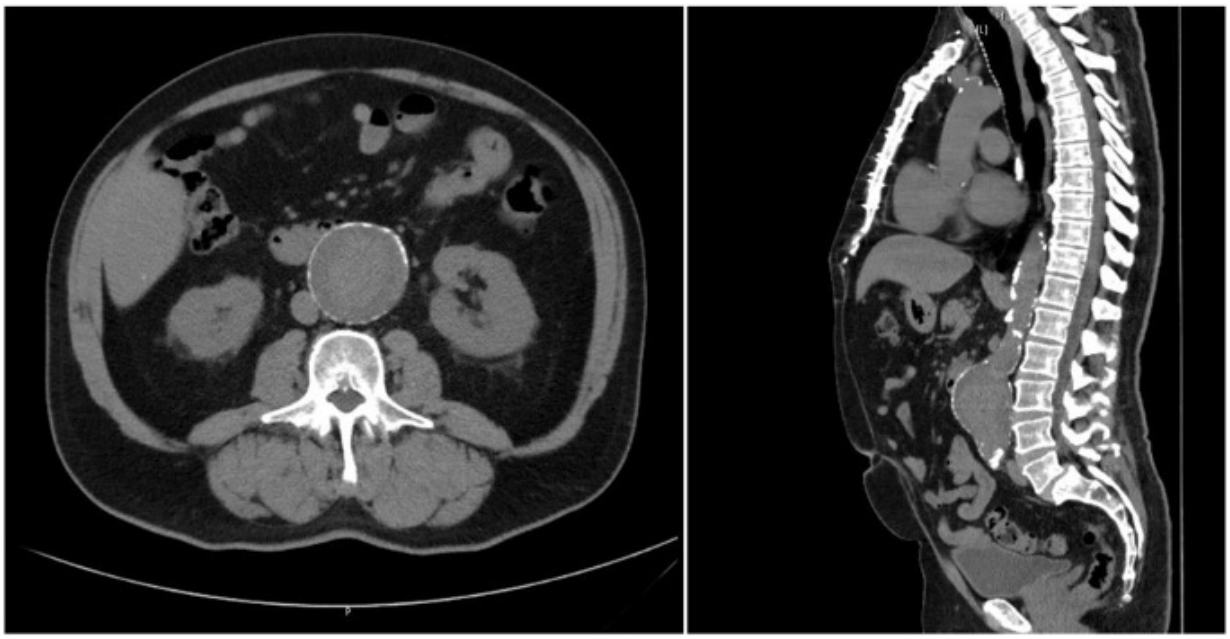


Figure 1. 11 *CT axial (left) and sagittal (right)views of AAA.* *(Kostun & Malik, 2016)*

1.6.2 Magnetic Resonance Imaging (MRI)

MRI is less widely used than CT, but an important imaging modality when AAA management requires repeated imaging given that it does not expose the patient to ionizing radiation or contrast agent. It provides precise anatomical information allowing for reliable assessment of AAA size, shape, and position (Figure 1.12) (Wanhainen et al., 2019)

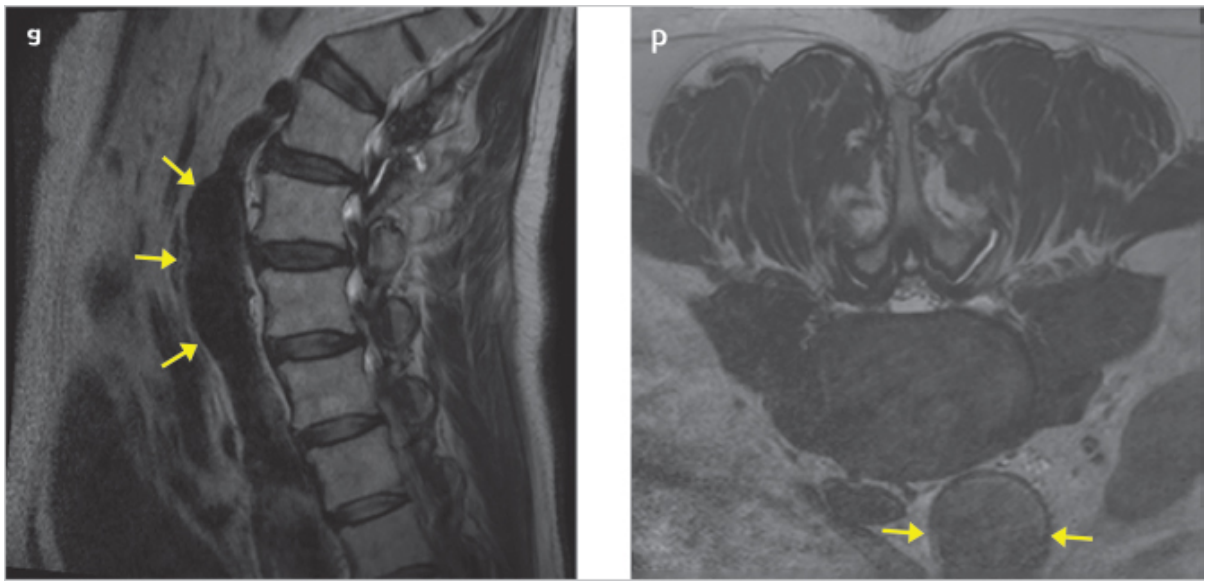


Figure 1. 12 *Sagittal (a) and transverse (b) MRI views of an infrarenal aortic aneurysm (yellow arrows).* (Radiology key. *2023)*

Furthermore, MRI provides good soft tissue contrast and can reveal AAA problems such as intramural thrombus, mural calcification, and branch vascular involvement (Figure 1.13). Improved MRI techniques, such as contrast-enhanced and diffusion-weighted imaging, can improve AAA characterization (van Ooij, 2023). Moreover, it provides a non-invasive examination of the aorta wall, including wall thickness, inflammation, and fibrosis, which can give insights into disease progression and future rupture risk (Deshpande et al., 2021).

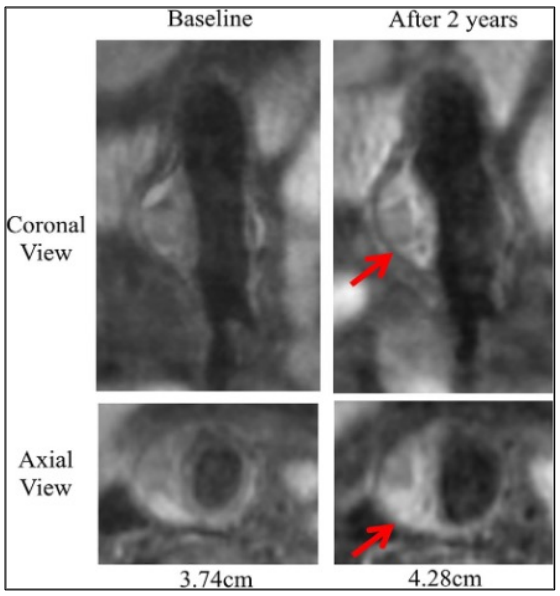


Figure 1. 13 *Intraluminal thrombus within AAA becoming bright showing fast growth over two years.* *(Deshpande et al., 2021)*

1.6.3 Angiography

Aortic aneurysm Angiography is an invasive diagnostic procedure that enables a comprehensive view of the abdominal aorta, offering important information on the aneurysm's size, location, and shape, and any related arterial stenosis or occlusions (Howell & Rabener, 2016). It involves the administration of a contrast agent into the bloodstream to enhance the visualization of the vascular networks and assists in treatment planning by giving a road map for endovascular treatments such as stent insertion or embolization. It has an important role as well after the Endovascular repair of AAA, as it allows clinicians to assess the position and integrity of the stent graft, ensuring that it is appropriately positioned and sealed within the aorta. Additionally, it helps in identifying any endoleaks, which are abnormal blood flow patterns outside the stent graft (Figure 1. 14). Endoleaks can cause aneurysm growth to persist and must be detected and treated as soon as possible. (Rosch et al., 1978)

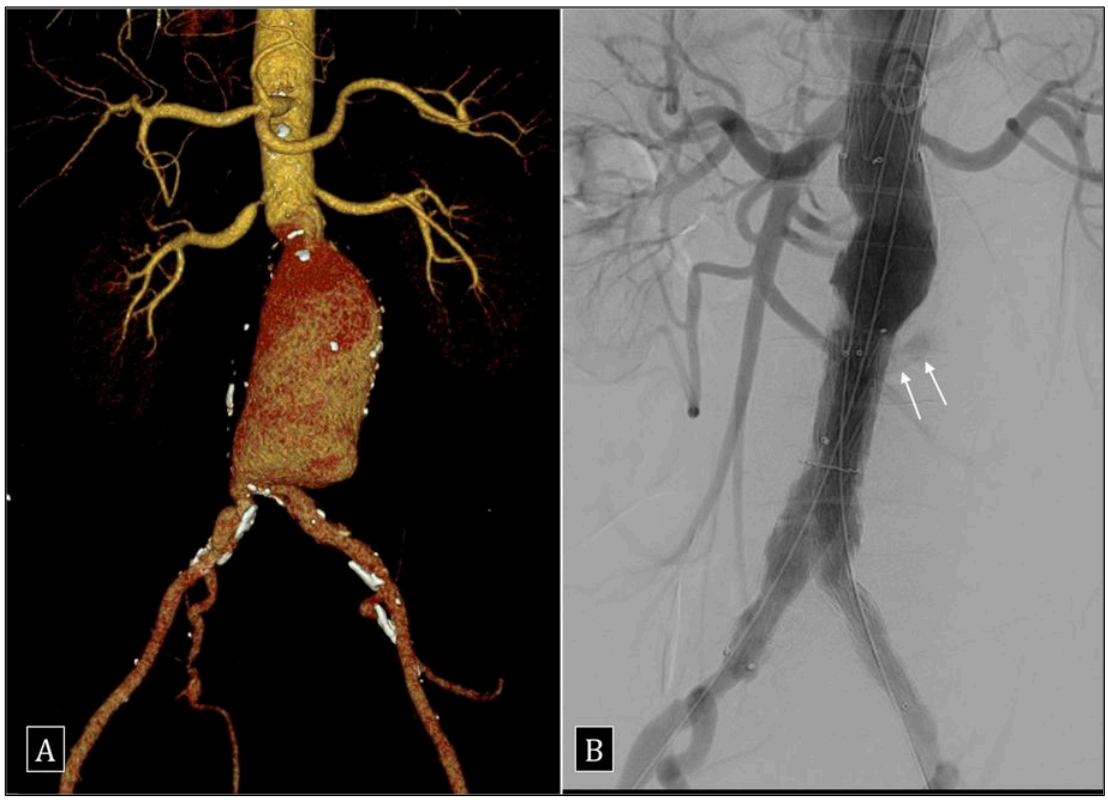


Figure 1. 14 *3D CT image (A) showing abdominal aortic aneurysm extending up to the bifurcation. Digital subtraction angiography image (B) showing good proximal and distal approximation of stent-graft with an endoleak near the carina (arrows).* *(Deshpande et al., 2021)*

1.6.4 Ultrasound

Ultrasound is considered a non-invasive, reliable, specific, sensitive, reproducible, low-cost, and minimally risky valuable screening tool for AAA, satisfying the WHO's criteria for an effective screening test. It remains the modality of choice, as it not only demonstrates high sensitivity and specificity in detecting AAA but also allows for the evaluation of the relationship between adjacent arteries -renal, mesenteric, and iliac- and the assessment of the arterial wall and the size of the intramural thrombus. (Frech et al., 2012) (Kostun & Malik, 2016) .

1.6.4.1 B-mode

Several studies have shown that B-mode ultrasonography is beneficial in detecting aortic aneurysms and other aortic diseases. B-mode has a 95% sensitivity and 99% specificity for detecting aortic aneurysms and can measure the size of the aneurysm as well as the presence of an intramural thrombus within. (Lederle, F. A. et al, 1997). A standard ultrasound technique was designed and validated to minimize the great variability in ultrasound-based AAA size estimates in clinical practice. The suggested ultrasound methodology is straightforward, involves minimal technical skills, and allows for immediate visual feedback during image acquisition. This technique involves placing the patient in a supine position or in a lateral supine position in an obese patient; to shorten the distance from the probe to the aorta, the abdominal aorta is centered in the screen, and it scanned axially to locate the largest diameter, the depth, and focus are adjusted. The probe is turned to a longitudinal view with the head of the transducer parallel to the longitudinal axis of the aorta while avoiding excessive compression that might decrease the diameter. The maximum diameter is determined, and an image is acquired during systole. Anterior-posterior (AP) diameter is measured with calipers placed on the inner-to-inner (ITI) vessel wall. The transducer is rotated 90 degrees to axial view at maximum diameter, an axial AP measurement is acquired. The same method is repeated twice, and the mean of three measurements is recorded (Tomee et al., 2021)**.** Figure 1.15 Provides a visual presentation of the correct ultrasound measurement of the aortic aneurysm.

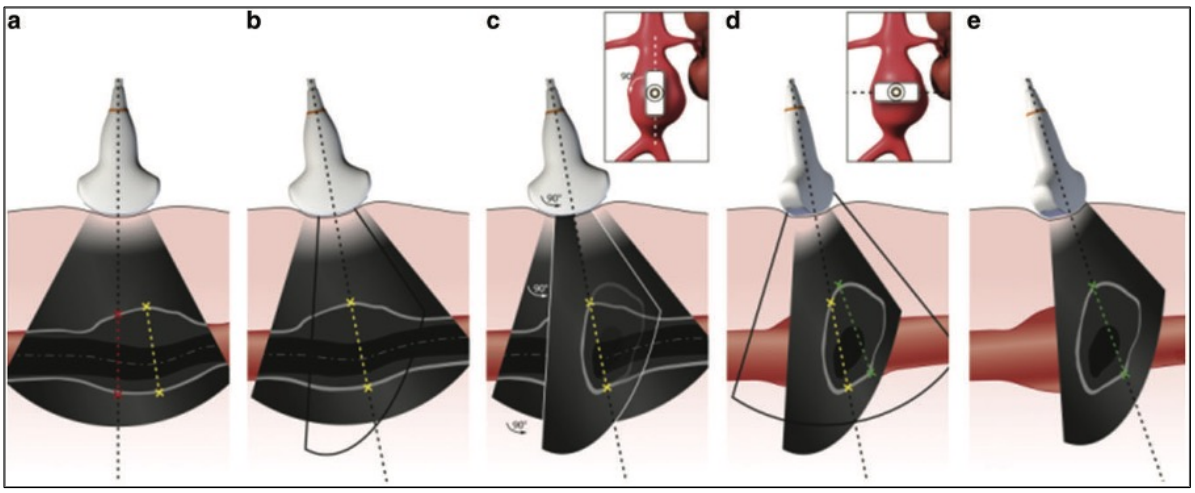


Figure 1. 15 *A guide to the correct ultrasound measurement. a) longitudinal view of aorta, b) transducer parallel to aorta axis, c) longitudinal anteroposterior (AP) measurement, d) transverse view of aorta, e) Transverse AP measurement.* *(Tomee et al., 2021)*

A variation in measurement approaches was noted in current screening programs, the National Health Abdominal Aneurysm Screening Program (NAAASP) uses the inner-to-inner (ITI) measurement method, the Swedish screening program uses the leading-to-edge-to leading edge (LELE) method, and the USA program not specifying which method was used (Figures 1.16). This variation in approaches may lead to sub-threshold aortas, as the ITI method underestimates the aortic diameter by 4mm when compared to the outer-to-outer (OTO) method (Figures 1.17). To address sub-aneurysmal aortas measuring 2.5-2.9 cm in Sweden, they were rescanned for surveillance every 5 years (Benson et al., 2018). Therefore, the inner-to-inner measurement approach has been shown to have higher reliability and reproducibility compared to the outer-to-outer measurement method. The choice of caliper placement method significantly affects the prevalence of AAAs in screening programs (Borgbjerg et al., 2018).

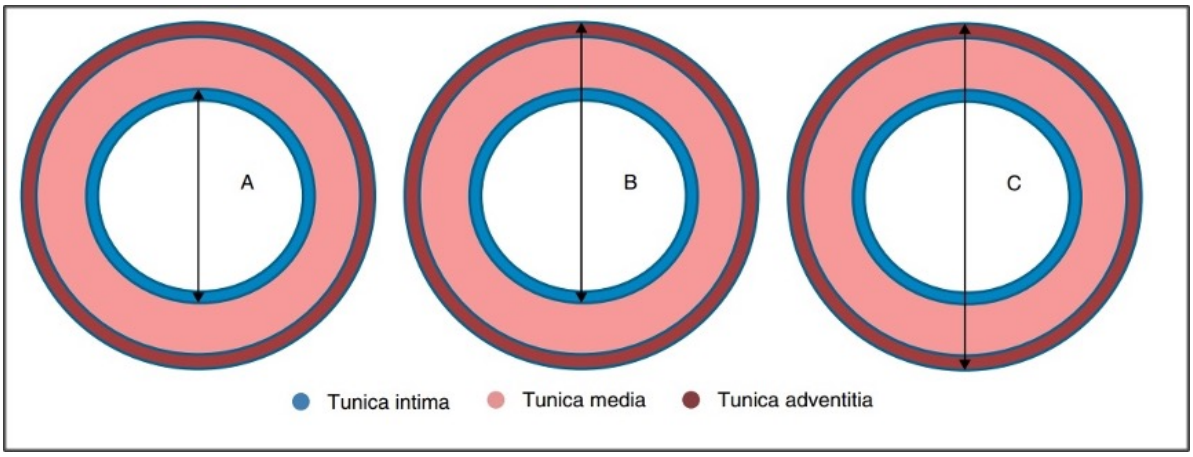


Figure 1. 16 *is a schematic representation of the three most common aortic diameter measurement approaches, with a) inner to inner (ITI), b) outer to inner (LELE), and c) outer to outer (OTO).* *(Beales et al., 2011)*

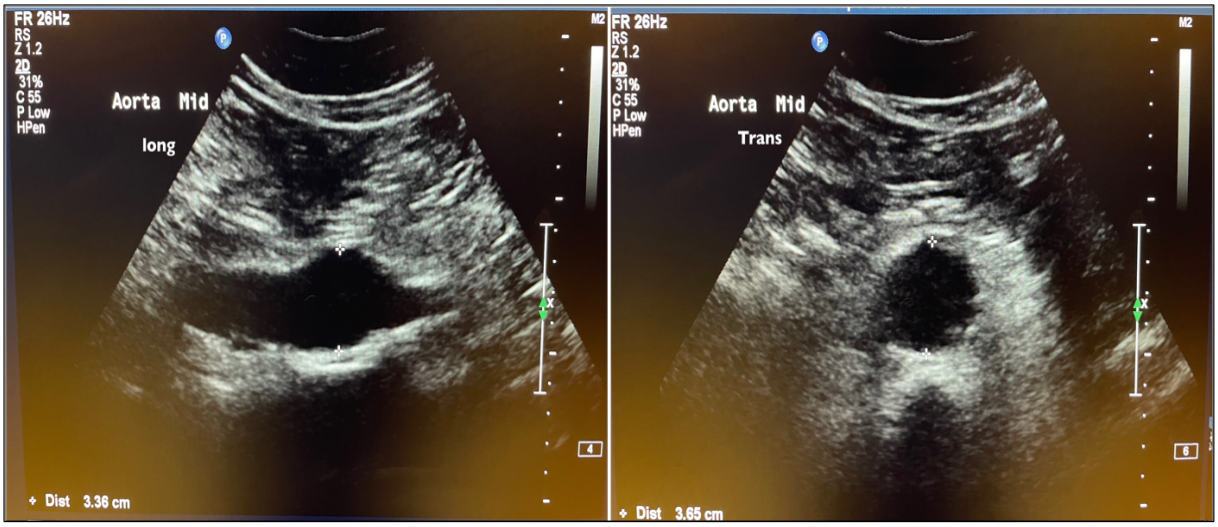


Figure 1. 17 *B-mode ultrasound images of a fusiform Abdominal Aortic aneurysm (AAA) in a 69-year-old male patient, demonstrating the inner to inner (ITI) measurement method.*

Some studies recommend using a CT scan for patients with AAA > 5 cm, as ultrasound tends to underestimate the size by 0.2 ± 0.3 cm (Figure 1.18). While CT angiography is the standard imaging method for pre-operative planning and surveillance after AAA repair, it is not suitable

for screening, given its high cost and the use of ionizing radiation and constant media (Kostun & Malik, 2016).

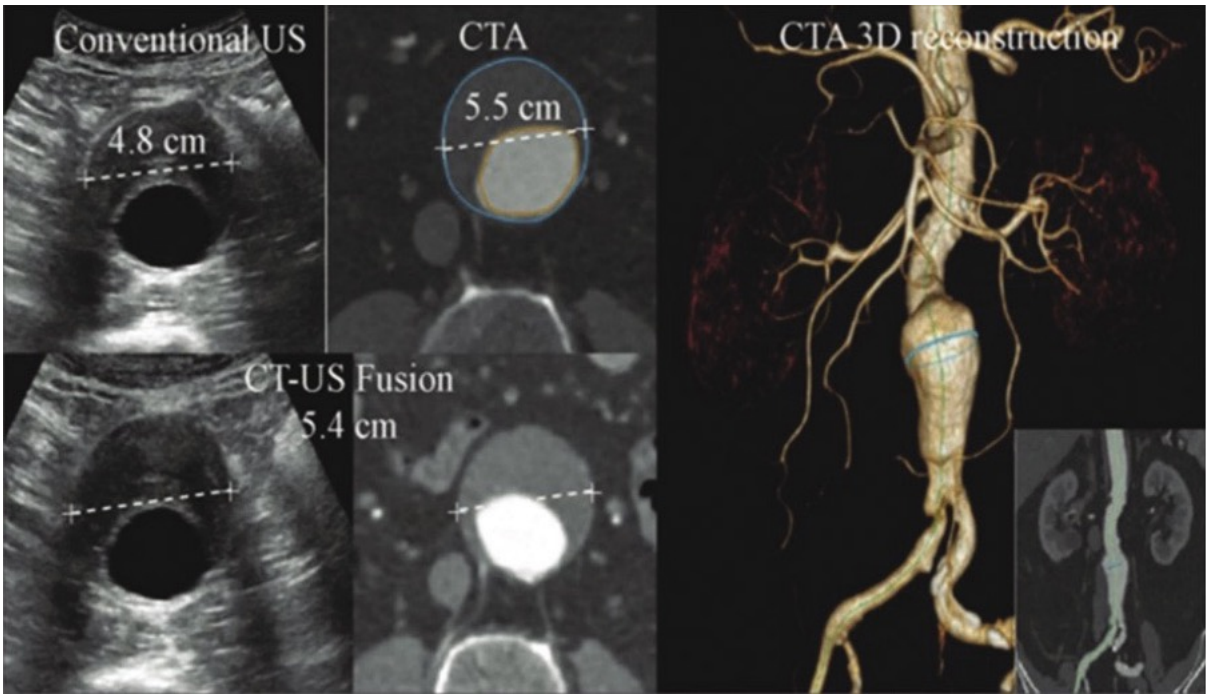


Figure 1. 18 *shows CT-US fusion measurements with related pictures along the same arterial plane.* (Sauceda, 2021).

1.6.4.2 Color mode

Color mode allows for visualizing blood flow direction and identifying flow disturbances such as helical or swirling flow patterns (Figure 1.19). These abnormalities in flow may be related to increased stress on the artery walls and an increased risk of aneurysm enlargement or rupture, aneurysms usually present with swirling flow. In addition, color Doppler is utilized to look for branches and thrombus within the aneurysm (Figure 1.20). The entire aneurysm is scanned in order to determine the location and type of any branches, as these are important to detect during

and after aortic aneurysm treatment because they may continue to be a source of flow into the aneurysm and a source of type II endoleak following endovascular repair (Battaglia et al., 2010)

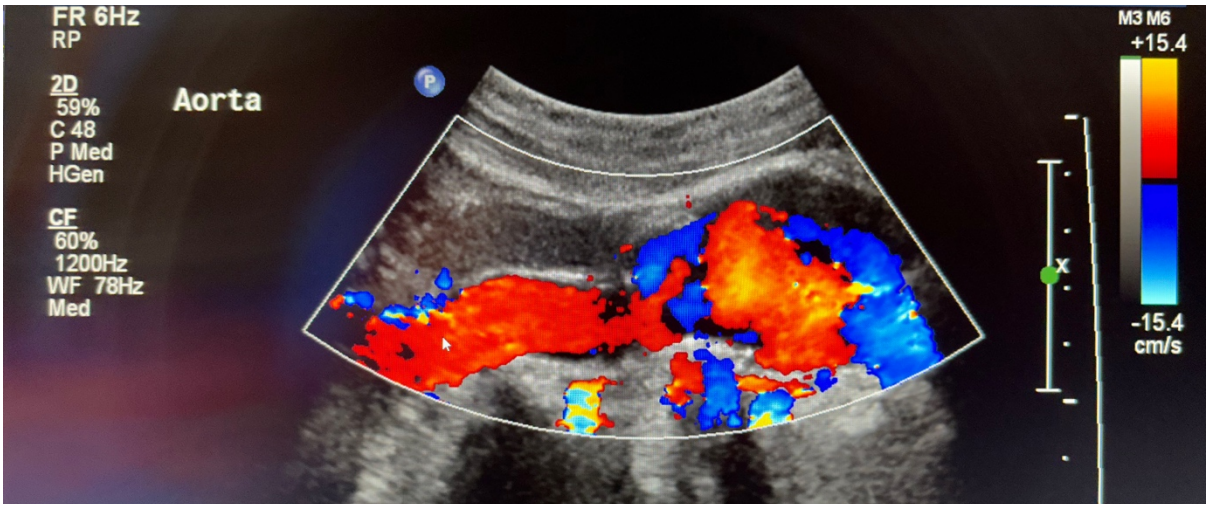


Figure 1. 19 *Swirling flow pattern within an aneurysm.*

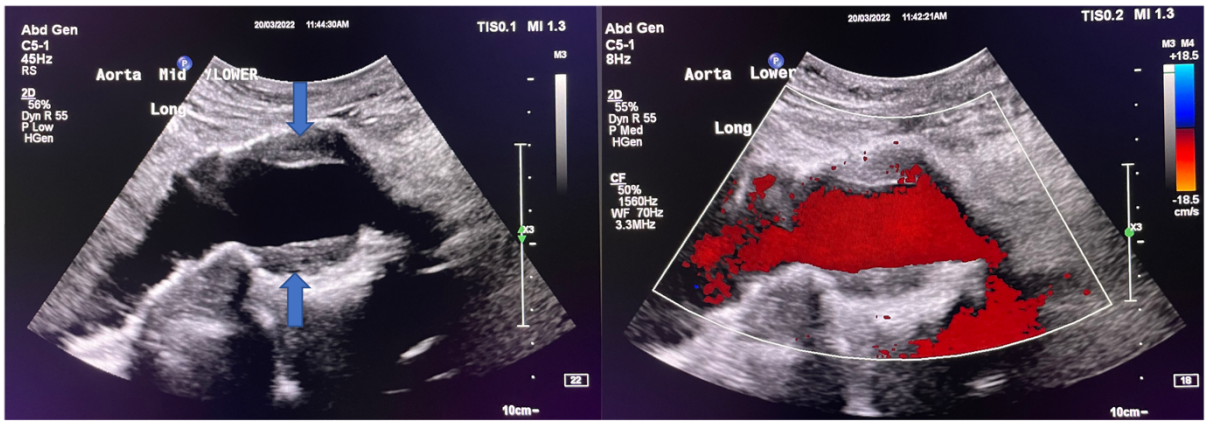


Figure 1. 20 *Aneurysm with an intramural thrombus at the anterior and posterior walls (arrows) on B-mode image (left) and color image (right).*

1.6.4.3 Spectral mode

The peak systolic velocity (PSV) within the aneurysm is one of the essential parameters assessed using spectral ultrasonography. PSV is a reliable indicator of blood flow velocity and is frequently used to determine the severity of stenosis or occlusion (Figure 1.21). PSV can

help with the detection of turbulent flow zones in AAAs, which may suggest stenosis or areas prone to rupture. Aneurysms are usually present with decreased linear flow velocities. A low-resistance flow pattern, as seen in spectral ultrasonography, indicates aneurysm expansion or the formation of collateral arteries. In addition, doppler ultrasound provides high levels of endoleak characterization by providing information on the direction of endoleaks and the velocity of blood flow. (Stickley & Meier, 2017).

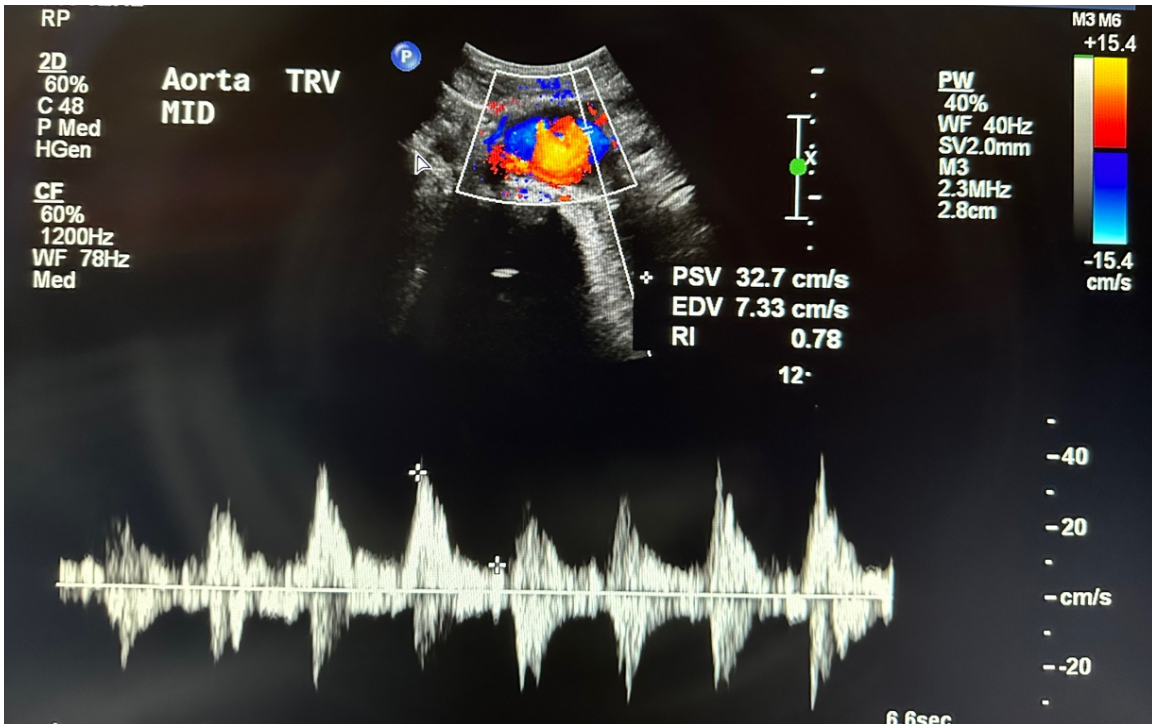


Figure 1. 21 *Spectral doppler ultrasound of an aneurysm showing the peak systolic velocity.*

1.6.4.4 Shear Wave Elastography (SWE)

Shear wave elastography (SWE) is a relatively recent imaging technique that offers significant information on tissues mechanical properties and stiffness such as abdominal aortic aneurysms (AAAs). SWE uses ultrasound to generate and analyze shear waves inside tissues, providing quantitative information on tissue elasticity. To create a shear wave, an acoustic radiation force push pulse, also known as an acoustic radiation force impulse (ARFI) push pulse, is used

(Sarvazyan et al., 1998).This shear wave propagates perpendicular to the push pulse and can be seen utilizing ultrafast plane wave acquisitions as it passes through the tissue (Figure 1.22). According to Young's modulus (YM), which measures the elasticity of the tissues, the speed at which it propagates is closely related. The harder the tissue, the greater the YM and the greater the shear wave velocity (SWV) (Shiina et al., 2015; Voizard et al., 2020a). In the setting of AAAs, SWE may help estimate the stiffness and structural integrity of the aneurysmal wall, which is crucial for estimating the risk of rupture. (Bertrand-Grenier et al., 2017) .

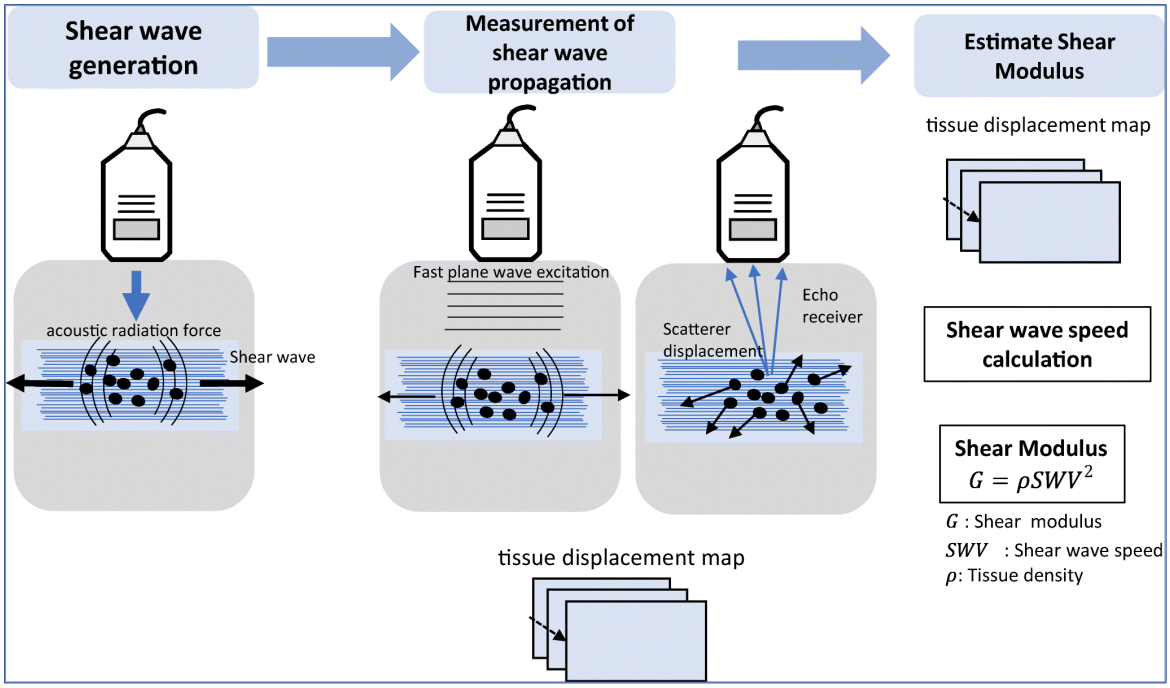


Figure 1. 22 *Physical principle of shear wave elastography.* *(Prado-Costa et al., 2018)*

1.6.4.5 Butterfly iQ probe

The Butterfly iQ probe is an emerging medical instrument that has improved the area of ultrasound imaging. It is a portable, affordable, compact, and lightweight ultrasound probe that

links to a smartphone or tablet, making it extremely accessible and simple for medical practitioners (Figure 1.23). It is powered by a single silicon chip that stores thousands of small acoustic transducers, allowing it to perform a wide range of diagnostic imaging applications. Its mobility, allows it to scan a wide range of human organs and systems, including the heart, abdomen, and musculoskeletal system, allowing for more rapid and accurate diagnosis while improving patient care (Baribeau et al., 2020).



Figure 1. 23 *portable Butterfly iQ probe bag.*

1.7 Treatment

1.7.1 Risk factor modification

Modifying risk factors is an essential step in preventing and managing abdominal aortic aneurysm (AAA). This involves several main strategies, such as quitting smoking, this involves several main strategies, such as quitting smoking, the most significant modifiable risk factor. Current smoking is associated with an increased AAA growth rate, and smoking cessation is likely to be associated with a 20% reduction in growth rate as well as a halving of the risk of AAA rupture (Thompson et al., 2013). Furthermore, treating high blood pressure through

lifestyle modifications and medication can help reduce the chance of developing an aneurysm. Following a healthy diet low in saturated fats and cholesterol and frequent exercise will help maintain a healthy weight, preventing the progression of AAA and many other diseases (Wanhainen et al., 2019).

1.7.2 Surveillance

Abdominal aortic aneurysm (AAA) surveillance is critical in managing and preventing this potentially fatal disease. Frequent monitoring enables the early detection of aneurysm growth or other size changes, which aids in determining the best time for intervention. Periodic ultrasonography examinations, which provide reliable and non-invasive assessments of the aneurysm's diameter and morphology, are the most popular technique of surveillance. The surveillance period is determined by the aneurysm's initial size, with smaller aneurysms requiring less frequent monitoring (Benson et al., 2018). The recommended surveillance regimen by the National Health Services Abdominal Aortic Aneurysm Screening Program (NAAASP) is illustrated in Figure 1.24. Frequent monitoring allows clinicians to detect rapid aneurysm growth, suggesting an increased risk of rupture, requiring urgent intervention and perhaps preventing fatal outcomes (Conway et al., 2012) (Thompson et al., 2012).

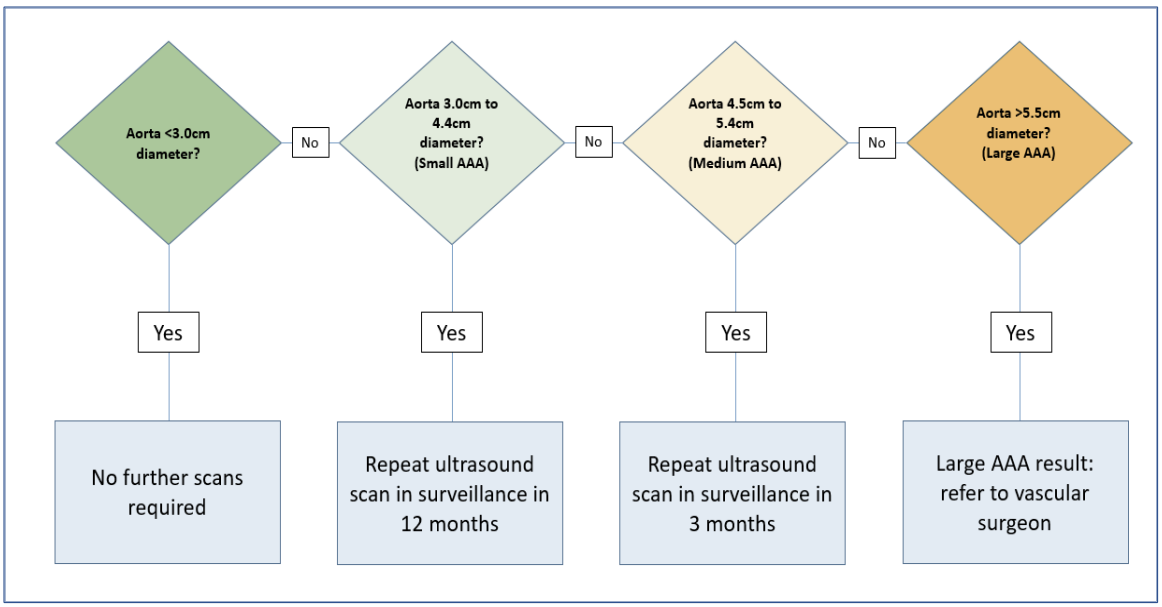


Figure 1. 24 *Surveillance of AAAA applied in NAAASP.*

1.7.3 Open surgical repair (OSR)

Open surgical repair remains a standard and effective treatment option for abdominal aortic aneurysms (AAA). A surgical incision in the abdomen is made to expose and repair the aneurysm using a synthetic graft. Open repair is often suggested for more giant aneurysms, complicated anatomical configurations, or individuals, not endovascular repair candidates. The operation includes temporarily interrupting blood flow by clamping the aorta above and below the aneurysm. The aneurysm is then opened, and the diseased aorta section is replaced with a graft that is stitched in place. Blood flow is restored, and the incision is closed after the graft is securely in place (Figure 1.25). Open surgical repair offers long-term outcomes with minimal aneurysm recurrence rates. It is, however, an invasive operation with risks such as bleeding, infection, and extended hospital stays. The recovery period following open repair is often greater than that of endovascular procedures (Wanhainen et al., 2019). It was reported that the 30-day or in-hospital mortality rate following open AAA repair was 4.1%. with an average

AAA diameter at surgery of 6.1 cm, and a mean age of 71 years. Post-operative renal failure affected 14% of the patients. but in 3% of patients, lifelong dialysis was required. Despite advances in endovascular repair, open surgical repair remains a viable therapeutic option, particularly for certain patient demographics and anatomical concerns (Rao et al., 2015).

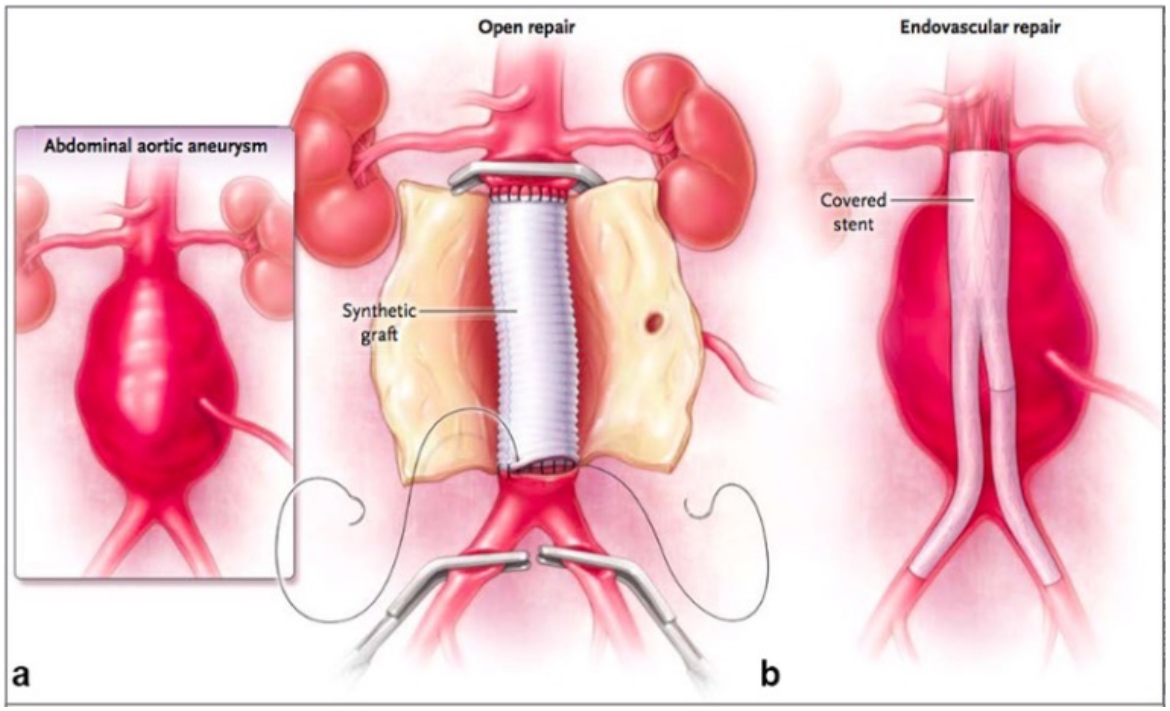


Figure 1. 25 *Infrarenal aortic aneurysm repair techniques a) open repair B) endovascular repair (EVAR).* *(Benson et al., 2018)*

1.7.4 Endovascular Aortic Repair (EVAR)

Endovascular repair for abdominal aortic aneurysms has become as a less invasive option to open surgical repair (AAA). This minimally invasive treatment involves placing a covered stent graft into the AAA aorta to strengthen the damaged artery wall and divert blood flow, thus removing the aneurysm from circulation. The stent is inserted through the common femoral arteries and it is fixed to the normal aorta above the aneurysm and the iliac arteries

below, using either radial force from the spring-mounted fabric or supra-renal fixating hooks (Figure 1.26) (Benson et al., 2018). Endovascular repair is often done through tiny groin incisions that enable access to the blood vessels. The stent graft is pushed through the blood arteries and placed at the site of the aneurysm using fluoroscopic guidance. The stent graft creates a new blood flow pathway, bypassing the weakened location and lowering the chance of rupture. Endovascular treatment has several advantages over open surgery, including less operating trauma, shorter hospital stays, less blood loss, and faster recovery times. It is especially useful for elderly patients or those with severe comorbidities who may not handle open surgery adequately. Almost all of the data implies that EVAR has a significant short-term survival advantage versus open surgical repair (OSR), with a similar long-term prognosis up to 15 years of follow-up. However, there is evidence that a higher likelihood of problems may arise beyond 8-10 years with previous generation EVAR devices, as well as uncertainty about the longevity of modern devices, particularly low-profile devices. As a result, EVAR should be regarded the primary treatment modality in the majority of patients. however, depending on the size, location, and anatomical features of the aneurysm, endovascular treatment may not be appropriate for all individuals. it is fair to recommend an OSR first strategy in younger, fit patients with a long-life expectancy >10-15 years as normal (average) survival after elective AAA is about 9 years (Wanhainen et al., 2019). Long-term monitoring is required to guarantee the stent graft's durability and proper function. Overall, endovascular repair has transformed AAA therapy by offering a less invasive approach with positive results for qualified patients.

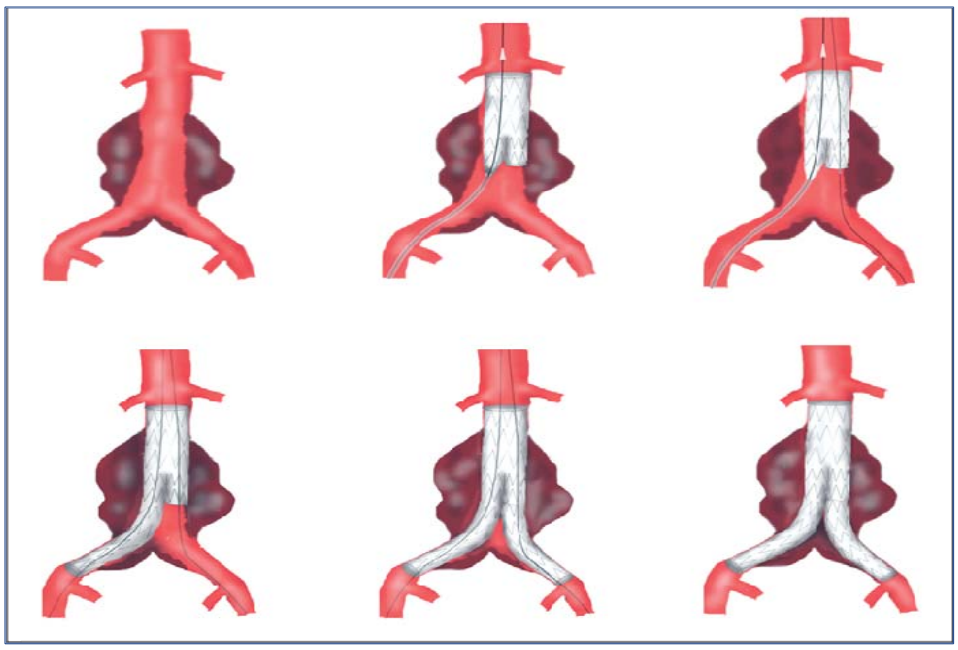


Figure 1. 26 *Endovascular aortic repair (EVAR) procedure.* *(Greiner, Grommes & Jacobs, 2013)*

1.8 Rationale for current study

1.8.1 Introduction

Abdominal aortic aneurysm (AAA) is characterized by a permanent, abnormal focal dilatation in the wall of the Abdominal aorta, typically exceeding 3 cm in diameter (Figure 1.1). The normal diameter of the aorta in adults is 2 cm at the diaphragm level, decreasing as it descends to 1.5 cm before bifurcating into the iliac arteries. (Erbel et al., 2014). The risk of aneurysmal rupture is directly proportional to the aneurysm diameter, with aneurysms measuring 5.5 cm or greater being at high risk of rupture (Lederle, Frank A. et al., 2002). AAA can be diagnosed incidentally during examinations for other diseases or via a screening program, as most aneurysms remain silent and asymptomatic until they rupture; at the time of rupture mortality rates are high, exceeding 80% before reaching the hospital (Reimerink et al., 2013) . In

contrast, early diagnosis and management of the disease can provide high survival rates, greater than 95%. Symptoms indicative of AAA can resemble those of other medical conditions, including appendicitis, cholelithiasis, diverticular disease as well as ureteric or musculoskeletal back pain, leading to potential misdiagnosis. A palpable pulsatile abdominal mass in the epigastric and left hypochondriac region with pain radiating to the back is the most classical patient presentation(Chaikof et al., 2009). However, these signs are often noted at the late stages of the aneurysm development and the pulsatility is linked to the rupture of the aneurysm. Mycotic or inflammatory AAAs, which account for about 0.65-2% of all AAAs, present additional symptoms such as fever, elevated inflammatory markers, and weight loss (Robertson & Bown, 2018) . Physical examination is unreliable and of poor detection sensitivity, with only 40% of AAAs being diagnosed in non-obese patients, and the diagnosis is highly dependent on the experience of the examiner and the body habitus of the patient. (Howell & Rabener, 2016) (Robertson & Bown, 2018).

1.8.2 AAA pathogenies

The underlying mechanism of abdominal aortic aneurysm (AAA) formation is complex (Figure 1.27), and the exact cause remains unclear. It is thought that both genetic and environmental factors, such as: smoking, hypertension, and visceral adiposity, have been implicated in its pathogenesis. The pathophysiology of AAA formation involves three primary mechanisms: proteolysis resulting from oxidative stress, inflammation, and loss of smooth muscle cells (SMCs). Oxidative stress increases by several risk factors of AAA, such as smoking and hypertension, contributing to proteolysis. During proteolysis, the enzymes matrix metalloproteinases (MMPs) and cathepsins cause the erosion of elastin and collagen in the extracellular matrix (ECM) of the vessel wall, leading to its weakening. Inflammation is driven

by macrophages and other inflammatory cells, which produce cytokines and reactive oxygen species that further degrade the ECM. The loss of the SMCs in the elastic wall lamina further weakens the vessel wall, making it more susceptible to dilatation and aneurysm formation (Stather et al., 2014) (Death et al., 2003) (Carino et al., 2018)

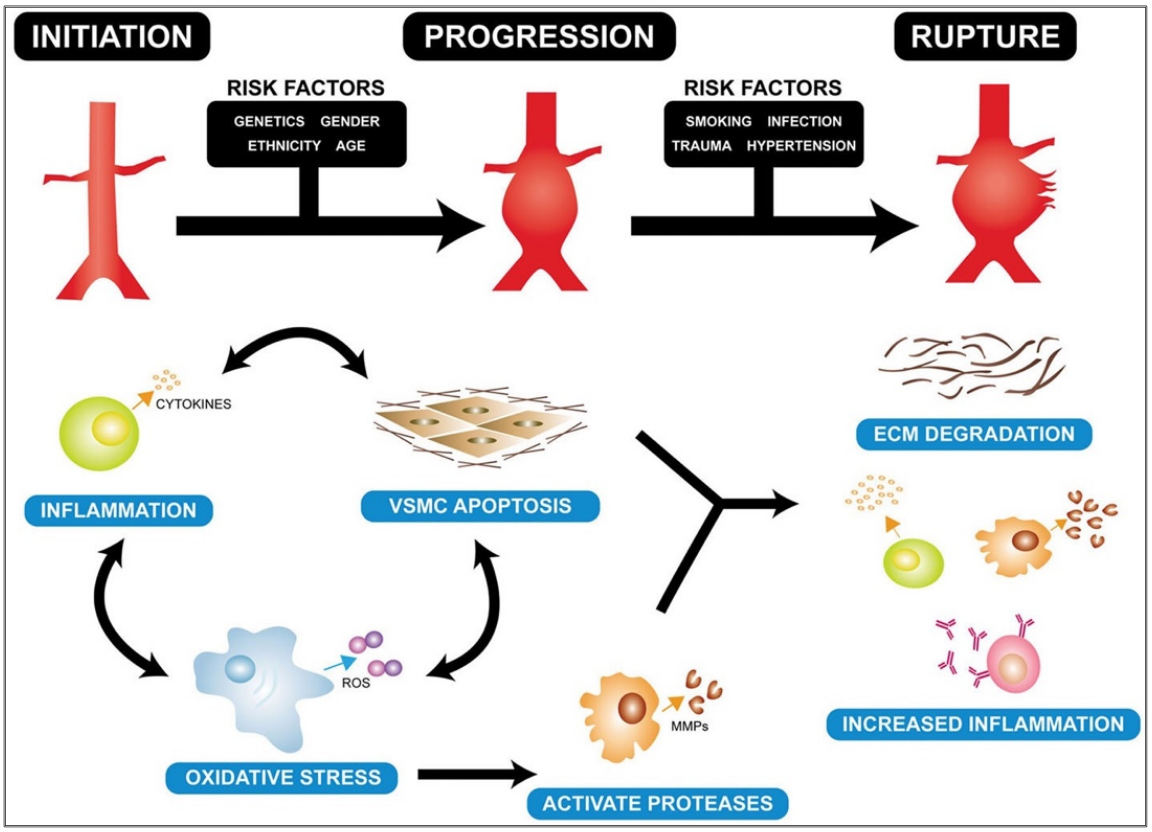


Figure 1. 27 *The process of Abdominal Aortic Aneurysm (AAA) pathogenesis (Kuivaniemi et al., 2015). Abbreviations: Extracellular matrix; MMPs: Matrix metalloproteinases; ROS: Reactive oxygen species; VSCM: Vascular smooth muscle cell.*

1.8.3 AAA Risk factors

The etiology of aneurysm is believed to involve a combination of genetic and environmental factors, with the genetic factor being supported by the higher incidence of AAA in first-degree relatives. Previous studies have established a consensus that AAA is associated with independent risk factors such as smoking, advanced age, family history, and male gender (Figure 1.3). (Alcorn et al., 1996) .Smoking is acknowledged as the strongest and most powerful modifiable risk factor for AAA, supported by several studies (Eiman Jahangir et al., 2015) (Howard et al., 2015) (Altobelli et al., 2018).The risk of developing AAA positively correlates with the number of cigarettes smoked and the number years of active smoking (Greco et al., 2010) . It was reported that current smokers face a 13.3 -fold increase in the risk of AAA, while former smokers face a 4.7-fold increase (Gentille-Lorente & Salvadó-Usach, 2011). Notably, numerous studies have demonstrated the association between the reduction of cigarette consumption and a decline in AAA prevalence (Laroche et al., 2015). A positive correlation was observed between smoking status and aortic diameter, with smokers exhibiting a larger aortic diameter than non-smokers (Altobelli et al., 2018) . Hypertension has been identified as the leading risk factor for AAA in women, with a comparatively lesser effect observed in men. Remarkably, the presence of hypertension was found to be associated with 93% of incident acute AAA events in women with a less observed effect among men (Howard et al., 2015).Male gender is an established non-modifiable risk factor for AAA, with a higher incidence reported in men than women. however, women are at four times higher risk of rupture once they develop it (Chaikof et al., 2009). Additionally, various medical conditions including hypertension, hyperlipidaemia, cardiovascular disease, atherosclerosis, and peripheral arterial disease have been found to significantly increase the risk of developing AAA (Figure 1.28)(Grøndal, Søgaard & Lindholt, 2015) (Eiman Jahangir et al., 2015).Previous

research has established a positive correlation between AAA and ischemic heart disease, with a high prevalence of AAA reported in patients with this condition. Conversely, the presence of AAA is related to higher incidence rates and greater severity of coronary artery obstructive lesions(Lipworth et al., 2012; Svensjö, S., Björck & Wanhainen, 2013). The development of AAA has been linked to aortic size, with individuals possessing a sub-aneurysmal aorta (2.5-2.9 cm) at age 65 having an increased risk of developing AAA within 5 years (Svensjö, S.|Björck, M.|Wanhainen, A, 2013) In addition, some studies have reported a positive association between waist circumference, indicating visceral adiposity) and the development of AAA (Carino et al., 2018). Conversely, other studies have pointed towards a protective effect of a BMI above >25m/kg^2 against the development of AAA , although the underlying mechanisms of this relationship remain unclear (Jahangir et al., 2015). However, Alpoloni et al have established that visceral fat cannot be used as a marker for the presence of AAA, and that there is no direct correlation between obesity and AAA.(Apoloni et al., 2019) Although diabetes Mellitus is an acknowledged risk factor for cardiovascular, cerebrovascular and peripheral vascular diseases, it is not considered a risk factor for AAA (Lederle, F. A. et al, 2000) Furthermore, several studies have consistently supported the protective role of diabetes in reducing the aortic aneurysm growth. (Jahangir et al., 2015) (Carino et al., 2018) (Antonopoulos & Liapis, 2018). This protective effect may be attributed to multiple aorta-protective mechanisms associated with diabetes mellitus (Antonopoulos & Liapis, 2018) .One of the most significant mechanisms underlying the protective effect of diabetes against aneurysm rupture is hyperglycemia mediated aortic stiffening, which reduce aortic wall stress. Hyperglycemia also plays a crucial role in decreasing degradation of the extracellular matrix (ECM) and in promoting the synthesis of smooth muscle cell, leading to a progressive increase in the volume of the ECM and the thickness of the vessel wall (Åstrand et al., 2007) . Another major contributing mechanism is the reduced level of matrix metalloproteinases (MMPs)

resulting from the aortic wall collagen network crosslinking induced by hyperglycaemia,which lowers the potential for aneurysm formation in diabetic patients (Death et al., 2003) (Golledge et al., 2008) However, it remains unclear whether this protection in such patients against aneurysm rupture is directly related to the changes in the aortic wall from diabetes mellitus or indirect, owing to secondary prevention and blood pressure control (Theivacumar et al., 2014).

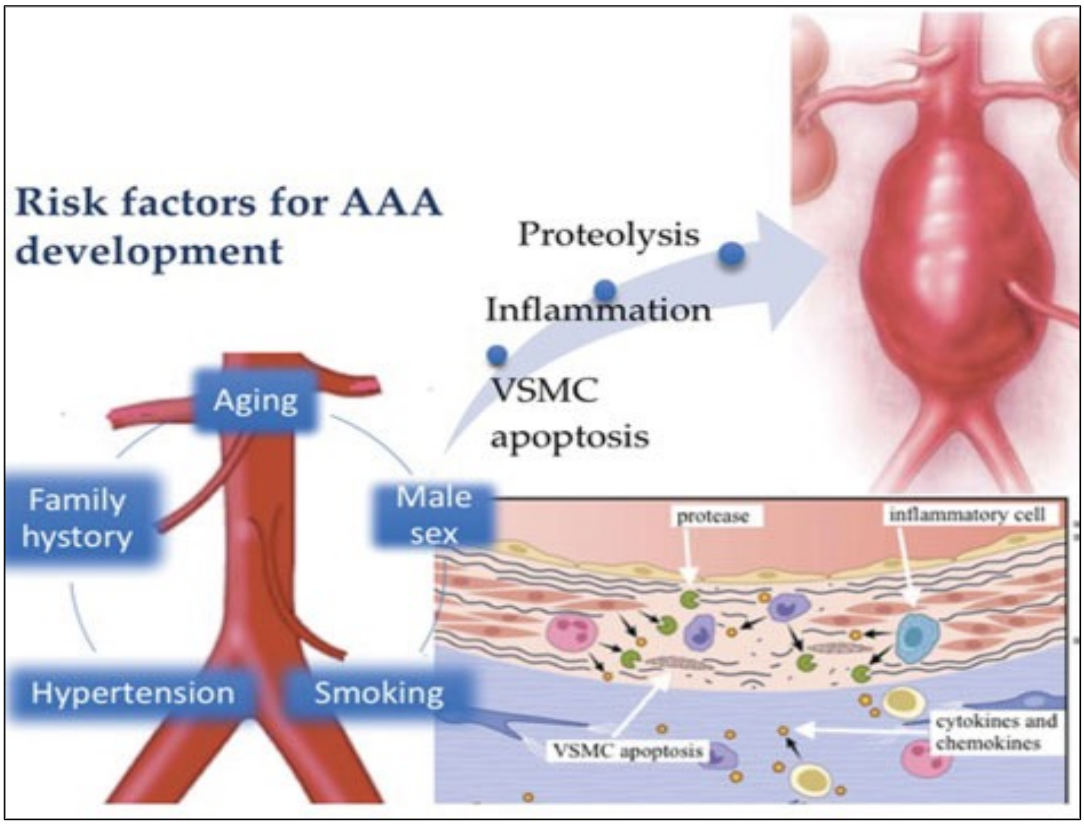


Figure 1. 28 *Main risk factors for AAA development, Abbreviations: VSMC: Vascular Smooth Muscle Cell (Carino et al., 2018).*

1.8.4 Smoking prevalence

Smoking continues to be an important factor contributing to early death and many disabilities. Globally, the reported standardized prevalence of daily smoking was 25 % for males and 5·4%

for females. Smoking prevalence has shown variations across different geographical locations, levels of development, and gender. (Reitsma et al., 2017). The incidence of smoking in Saudi Arabia, in comparison to other nations, has distinctive trends. Based on the data that is currently accessible, the incidence of tobacco use among the adult population in Saudi Arabia is comparatively elevated. The most recent National Health Survey carried out by the General Authority of Statistics revealed that the rate of smoking of any type of tobacco among adults in Saudi Arabia was 18 % among adults (15 years old and above) (General Authority of Statistics, 2023). Nevertheless, it is essential to acknowledge that smoking rates may range among various locations within the nation. When comparing Saudi Arabia to other nations, the prevalence of smoking may vary, either being higher or lower depending on the country being compared. Existing data collected between 2004 and 2012 reveals a notable prevalence of cigarette smoking among individuals with limited educational opportunities in four Arab countries, suggesting a fundamental association. Among these countries, high prevalence rates were observed among men, with rates of 51.3% in Syria, 39.7% in Palestine, and 42.1% in Lebanon. Among women, comparatively lower prevalence rates were recorded, with rates of 8.4% in Syria, 10.9% in Jordan, and 24.3% in Lebanon (Abdulrahim & Jawad, 2018). A systemic analysis of twenty studies that offered nationally representative prevalence data on current dual, or poly-tobacco use among people in 48 countries with the definitions of dual and poly-tobacco use showing significant variation among the studies, indicated that the occurrence of using many types of tobacco was more common in countries with lower economic status, namely low- and lower-middle-income nations, in comparison to countries that had higher economic status. Among men, the incidence of current dual usage of smoked and smokeless tobacco products ranged from 0.2% in Ukraine (2010) and Mexico (2009) to 17.9% in Nepal (2011). The prevalence of poly-tobacco usage among males varied from 0.8% in Mexico (2009) and 0.9% in Argentina (2010) to 11.4% in the United Kingdom and 11.9% in Denmark

in 2012. Dual tobacco consumption was typically more widespread in Southeast Asia, although the usage of several tobacco products was reported in both Europe and Southeast Asia (Chen et al., 2021).

1.8.5 Rational for the study

Although abdominal aortic aneurysms (AAA) are typically asymptomatic, the risk of rupture is a critical and often fatal outcome. Early detection of AAA is essential for reducing mortality rates and improving patient outcomes. Ultrasound is the preferred method for screening AAA due to its cost-effectiveness, accuracy, reproducibility, and lack of exposure to ionizing radiation or contrast agents. Additionally, it has superior sensitivity compared to clinical examination. Economic viability for screening is considered when the prevalence rate of AAA is 1% or higher. In Western countries, evidence-based studies have demonstrated that AAA screening in older men is cost-effective and reduces mortality rates from rupture. However, in Saudi Arabia, there has been limited research on AAA screening, despite significant social and economic changes in recent decades, including sedentary lifestyles, unhealthy diets, and increased sodium iodine consumption, which have been associated with obesity and the development of various diseases. Therefore, implementing a national AAA screening program may reduce the rate of death from AAA rupture, explore epidemiological risk factors associated with AAA development, and enable comparison with similar studies conducted on different ethnic groups in Western countries. However, the decision to approve such a program should be based on multiple factors, including the prevalence and morbidity rates of AAA, the associated costs, the capacity of hospitals to treat diagnosed individuals, and the budget allocated for healthcare services. This screening study aims to provide valuable information about the prevalence of AAA among the population of Saudi Arabia, specifically the residents

of Riyadh city, to establish screening guidelines suitable for the Saudi population. Shear wave elastography (SWE) ultrasound has the potential to provide valuable diagnostic and monitoring information related to the elastic properties of the abdominal aortic wall. By offering insight into the stiffness of the wall and facilitating a more accurate assessment of the risk of disease progression associated with AAA, using SWE in the assessment of the wall of the aorta can improve the practice of AAA detection, and provide better patient outcomes. Given that the cost and hospital capacity are important factors in deciding whether to approve an AAA screening program, handheld ultrasound devices, such as the Butterfly iQ probe, could be a viable option for mass screening. These devices are less expensive than conventional ultrasound machines and their small size and portability allow for screening in locations other than hospitals. Consequently, it would be beneficial to assess the efficacy and reliability of such devices in detecting and evaluating AAAs.

1.9 Research questions

1.9.1. Thesis Hypotheses

In the present study, it is hypothesized that the prevalence of abdominal aortic aneurysm (AAA) in Riyadh, Saudi Arabia is similar to that observed in western countries and that a national screening program would be cost-effective. Furthermore, that the wall of the aorta in aneurysms exhibits distinct elastic properties compared to non- aneurysmal aorta wall. Finally, the efficacy of the Butterfly iQ probe as diagnostic tool for evaluating aortic aneurysms was predicted to be comparable to that of a conventional ultrasound machine.

1.9.2 Aims and objectives

1. The primary aim of this study was twofold: firstly, to determine the prevalence of abdominal aortic aneurysm (AAA) in the elderly population of Riyadh city, with the aim of improving clinical practices for detecting AAA. Secondly, this study aimed to investigate the potential association between AAA and various risk factors, including age, smoking habits, gender, hypertension, hyperlipidemia, and cardiovascular disease.
2. The second objective is to examine the elastic properties of both aneurysmal and non-aneurysmal aortic walls utilizing Shear Wave Elastography (SWE) ultrasound.
3. The final objective of this study was to assess the reliability of the butterfly iQ probe as a diagnostic tool for evaluating aortic aneurysms and compare its efficiency to that of the conventional ultrasound machine.

CHAPTER 2: Literature Review

In this chapter, a comprehensive overview will be presented on the global burden of AAA, including its consequences. The historical background and benefits of AAA screening will also be discussed, along with the variability of screening programs worldwide. Additionally, the potential value of shear wave elastography in evaluation the aortic wall health will be reviewed, as well as the efficiency of using handheld devices for aortic scanning.

2.1 Global burden of AAA

In 2001, The Collaborative Aneurysm Screening Study Group (CASS) combined data sets from four separate randomized control trials for ultrasound screening of AAA in three countries (UK, Australia, and Denmark) to estimate the prevalence of AAA with greater statistical precision. The age-standardized prevalence of AAA ≥ 3 cm was reported as 4.5 %, 6.5%, 5.2 %, and 6.7% in Denmark, Australia, and the UK, respectively. The prevalence varied considerably among countries, with the highest being in the southern UK and the lowest in central Denmark. The CASS group attributed the higher prevalence in the UK to the earlier start of the trial in 1988 compared to the other trials and that the lower prevalence in Denmark to the indigenous population with low immigration rates in contrast to the western Australia population, which had high post-war immigration rates, in contrast to the Western Australian population, which had high post-war immigration rates from Europe. This finding suggests that ethnicity could be the cause of such differences since the age, gender, definition of AAA, and measurement method were the same in all four trials (Ashton et al., 2001).The prevalence and trends of AAA in the general population from 1988 to 2013 were assessed in a metanalysis of datasets from 56 randomized control trails, cross-sectional studies, and prospective cohort

studies. The overall pooled prevalence was 4.8%, being higher among males than females, with the highest percentage for the age group of 65-74 years. In terms of areas, Australia was ranked as having the highest AAA prevalence (6.7%) compared to Europe (2.5%) and USA (2.2%). The pooled prevalence in Western countries was higher than in Asian countries, namely Japan and Korea. However, the wide variation in prevalence among populations is expected due to several differences in studies, including AAA definitions, sex distributions, age, and risk factors. There has been a gradual decrease in AAA prevalence in Europe from 6.5% in 1988 to 2.5% in 2013. The authors speculate that the high reported prevalence rates in the past decades might be related to individuals' prolonged life spans in addition to the availability of diagnostic screening programs. (Xi Li et al., 2013) Similarly, in reviewing the trends of AAA prevalence and mortality in 18 non-European countries from 1983 to 2013, it was found that the prevalence rates varied greatly between countries being the highest in Australia and the lowest in Eastern Asia. Moreover, the reported rates varied among the population of the same country due to the different ethnic backgrounds. It has been shown that the prevalence of AAA in Brazil increased from 2.1% to 6%, indicating a trend of an increase in the AAA prevalence. The differences in the screened populations, methods of screening, disease coding systems, and limited data about AAA in developing countries have contributed to the variability in available information. The study concluded that establishing a clear standard screening method to diagnose AAA worldwide would be beneficial in providing epidemiologic data about the burden of AAA. (Munoz-Mendoza, Jerson|Pinto Miranda, Veronica A.|Quevedo, Henry C.|Hebert, Kathy, 2013). In the-first-of-its kind review article assessing the global burden of AAA disease in 21 world countries and regions over 20 years, it was reported that the prevalence rates of AAA per 100,000 declined from 2422.53 in 1999 to 2274.82 in 2010 among the age group of 75-79 years, with the highest decline rates being found in high-income countries. This decline in rates in developed countries might be related to the risk factor

modification programs provided by the health care systems, such as smoking cessation. Regardless of the global decline in rates, developing countries have shown a rise in the burden of AAA over that period, most likely due to increased tobacco consumption and the emergence of cardiovascular disease. These findings emphasize the importance of global improvements in the prevention, diagnosis, treatment, and surveillance data of AAA (Sampson et al., 2014). According to the most recent report on the global burden of AAA over the past two decades, the prevalence of AAA was 0.92% worldwide in 2019, with the western Pacific region having the highest prevalence (1.3%) and the African region exhibiting the lowest prevalence (0.33%)(Song et al., 2023).

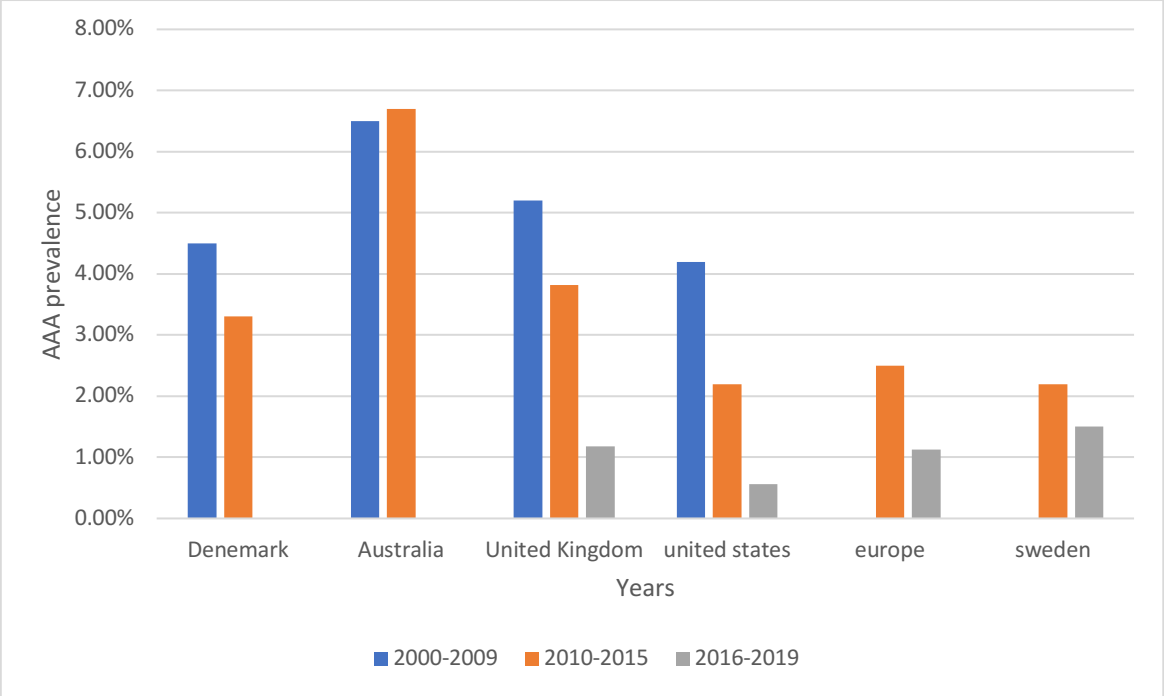


Figure 2. 1 *Change in Abdominal Aortic Aneurysm prevalence in developed countries over the past two decades.*

2.2. The value of detecting AAA

Several studies have demonstrated the value of detecting AAA through screening. The Multicenter Aneurysm Screening Study (MASS) study found that screening reduced the risk of death from AAA by 53% with a continuity of the benefits over 13 years after screening, in terms of a 42% reduction in the relative risk of AAA-related mortality and a 3% reduction in all-cause mortality (Scott, 2002) (Fleming et al., 2005). The U.S. Preventive Services Task Force (USPSTF) reported that inviting men aged 65 to75 years to AAA screening for AAA reduced AAA-related mortality by 43%, and screening 69% of men with a history of smoking prevented an estimated 89% of AAA-related deaths (LeFevre, 2014). The NAAASP found that in addition to being cost-effective and reducing AAA-related mortality, AAA screening provides the secondary benefits of improving the general health of those screened and modifying the risk of cardiovascular disease (Conway et al., 2012). Ali et al. found moderate evidence supporting the benefit of one-time screening of asymptomatic men aged 65 years or older. The study reported a reduction in the risk of AAA-related mortality by 43% and the risk of rupture by 48% after 3 to 5 years of follow-up and by 42% and 38%, respectively, after 13 to 15 years of follow-up. However, there was no significant benefit observed for screening women (Ali et al., 2016). Overall, screening for AAA has been shown to be effective in reducing AAA-related mortality and improving general health, particularly in high-risk groups such as men aged 65 years or older with a smoking history.

2.3. AAA Screening

2.3.1. Screening history and guidelines

The concept of AAA screening was established from a series of randomized control trials in the 1990s (Earnshaw, J. J. & Lees, 2017). In 2002, the Multicenter Aneurysm Screening Study (MASS), one of the largest clinical randomized control trials with the narrowest confidence intervals, provided reliable evidence supporting the implementation of a national screening program for AAA. This Four-year randomized control trial involved 67 800 men aged 65-74 from four centers in the UK, divided into a control group and a screened group. Participants' abdominal aortas were scanned using ultrasound to detect aneurysms, and those who didn't have aneurysms were not followed up, while those who were found to have aneurysms were followed up annually if the aortic diameter measured 3-4.4 cm or every three months if the aortic diameter was 4.5-5.4 cm. Symptomatic patients, with an aortic diameter of 5.5 cm or greater or with a rapid aortic expansion rate of 1cm/year were urgently referred to a vascular consultant. Aneurysm-related mortality in this sample was assessed over a four-year period. Results showed that screening reduced the risk of death from AAA by 53% with 47 fewer deaths in the screened group compared to the control group (Scott, 2002). In terms of cost-effectiveness, the four-year analysis showed that an additional cost of £2.2 million was incurred in the screened group, with an adjusted net cost per patient of £36.39 and £28400 per life year gained (Multicentre Aneurysm Screening Study Group, 2002). The mortality benefit of screening remained consistent ten years following MASS, with a 48% reduction in AAA-related mortality and a cost-effectiveness ratio per life year gained of £7600, which is below the value set by NHS guidelines per life year gained (25000£) (Thompson et al., 2009). The final report on AAA screening after 13 years of follow-up of the MASS showed the continuity of the benefits of screening in terms of a 42% reduction in the relative risk of AAA-related

mortality and a 3% reduction in all-cause mortality. Although the benefit of AAA mortality risk reduction declined 13 years after MASS compared to those 10 years after randomization, the overall benefit-to-harm balance remains in favor of screening. To save one death over 13 years, the number of men screened needs to increase by an estimate of 216. An increase in the incidence of AAA ruptures in the screened group with an original normal scan was noted, most of these ruptures occurring after seven years in patients with baseline aortic measurement of 2.5-2.9 cm. A proposed solution was to include those with a sub-aneurysmal aortic diameter of 2.5 to 2.9 cm in surveillance once after five or seven years of the initial scan (Thompson et al., 2012).In 2005 a review of the benefits and harms of AAA screening was conducted for the U.S. Preventive Services Task Force (USPSTF), an independent panel of primary care physicians and non-federal experts in methodology and health behavior who developed screening guidelines in coordination with the systematic review sponsored by the Agency for Health Care Quality. The review included Four randomized control trials evaluating the population-based screening for AAA: The Multicentre Aneurysm Screening Study (MASS) in the United Kingdom, the Chichester, United Kingdom screening study, the Viborg County, Denmark screening study and the Western Australia screen study. Data from these trials were pooled and used for the metanalysis. Based on the analysis results, the authors indicated that AAA-related mortality is reduced by 43% in men aged 65 to 75 years invited to screening for AAA, and screening 69% of men with a history of smoking prevented an estimate of 89% of AAA-related deaths. The MASS study, being the largest with the narrowest confidence interval, contributed mostly the pooled estimates. No significant benefit was found in screening women for AAA as the disease is more prevalent in men. It was recommended to screen men aged 65 to 74 years with a history of smoking in the united states(Fleming et al., 2005). The USPSTF updated its 2005 recommendation on screening based on assessment of the balance of benefits and harms of AAA screening in published relevant studies from 2004 to 2013. The

recommendation applies to asymptomatic adults of age 50 years or older. It was concluded that one-time ultrasound screening for AAA in men aged 65-75 years who have ever smoked is supported by a moderate net benefit (B recommendation). Selective screening by clinicians based on risk assessment was recommended for men aged 65-75 years who have never smoked, as sufficient evidence supports that the benefits of screening are small given the low prevalence of AAA among them (C recommendation). There has been insufficient evidence on the balance of benefits and harms of AAA screening in women aged 65-75 years who have ever smoked, since only one trial included women which in turn was underpowered to draw conclusions related to gender. It is not recommended to screen women aged 65-75 years who have never smoked for AAA (D recommendation) as the harms of screening outweigh the risk for this group. The USPSTF defines "ever smoked" as smoking at least 100(LeFevre, 2014)(LeFevre, 2014). In England, the National Health Services Abdominal Aortic Aneurysm Screening Program (NAAASP) was implemented in 2009 based on data provided four years after MASS and followed the same protocols and procedures in which 65-year-men were invited for screening. It achieved full coverage of the entire nation by 2013 (Conway et al., 2012) However, it was noted that the prevalence of AAA varied greatly, being less than expected (1.5%) when compared to MASS (4.9%). As a result, concerns were raised about whether AAA screening was still cost-effective. A re-estimation of cost-effectiveness was carried out to answer this question. The original Markov model underwent several validation and recalibration processes to reflect contemporary costs. Surprisingly, the new modeling showed that AAA screening remained highly cost-effective. The incremental cost-effectiveness ratio (ICER) was £5758 per life year gained and £7370 per quality-adjusted life year (QALY) gained which is acceptable and well below the threshold set by the National Institute for Health and Care Excellence (NICE): 20000£ per QALY (Glover et al., 2014). In addition to being cost-effective and reducing AAA-related mortality, AAA screening provides

the secondary benefits of improving the general health of those screened and modifying the risk of cardiovascular disease. However, only some of the western countries have implemented national screening programs for the diagnosis of AAA, and other countries are considering the initiation of such programs. There are variations among existing programs in different aspects, such as the age group, small AAA imaging intervals, and the inclusion of women. There are no universally adopted guidelines(Rahal, Zuberi & Badgett, 2015). Although the Canadian society of Vascular Surgery recommended national or provincial screening for AAA, such a program didn't exist in Canada as the Canadian task force did not find enough evidence to support a screening program. In an attempt to update the previous 1991 recommendation on AAA screening of the Canadian Task Force on preventive health care Ali et al. created a report to provide guidelines for AAA screening with ultrasound. Consistent with previously published literature, the authors reported moderately significant evidence of the benefit of one-time screening of asymptomatic men aged 65 years or older in terms of reduction of the risk AAA related mortality by 43% and the risk of rupture by 48% after 3 to 5 years of follow-up and by 42% and 38%, respectively, after 13 to 15 years of follow-up; with no significant benefit of screening for women. limited evidence was found on the benefit of repeated screening and targeted screening based on risk factors. Most of the findings were similar to that of the USPSTF review, except for some differences. A Marginally significant benefit of one-time screening on all-cause mortality 13 to 15 years later was found, unlike to what was reported by the USPSTF review of no benefit. Similarly, the USPSTF review reported a reduction of 30-day post-operative mortality after emergency procedures in the screened group. Ali et al. showed that there is no difference in the 30-day post-operative mortality between the screened and control group. The authors reported evidence of over-diagnosis of men by 45% from MASS data, in which the diagnosed AAA would not have ruptured or required preventive surgery. Its observation was associated with significant anxiety for the diagnosed person (Ali

et al., 2016). Based on the evidence provided by the earlier Ali et al systemic review, the Canadian Task Force revised its 1991 recommendation on AAA screening for asymptomatic patients. It recommended one-time ultrasound screening for AAA in men aged 65 to 80, as the benefits of screening in terms of reduction in AAA mortality risk, rupture, and emergency procedures outweighed the harm of overdiagnosis in that age group. The Task Force recommended against screening men older than 80 years as the most of them are more likely to have medical conditions that limit their ability to undergo elective repair procedures and recommended against screening women due to low evidence of no benefit from screening women in addition to the high risk of death after AAA repair (Singh et al., 2017)(Singh et al., 2017).

In Denmark, from October 2008 to January 2011, the first randomized control trial of population screening for vascular disease (VIVA) in men aged 65-74 was carried out. The screening group was screened for AAA, PAD, and HTN diseases, and it was shown that they were prevalent by 3%,10.9%, and 10.5%, respectively, with an 11% overdiagnosis due to the high number of false positive diagnosis of HTN. It was observed that all-cause mortality was significantly reduced 5 years following the start of screening, which could be a contribution of both the diagnosis and pharmacological intervention. The authors concluded that combined screening is recommended as an alternative when it is difficult to establish population screening. (Lindholt & Søgaard, 2017). However, the VIVA trail was carried out free in a high-income country and might not be applicable in other lower-income countries, and the provided evidence is not sufficient, further research is needed to implement such a program. (Ayoub & Murad, 2017). Smoking cessation, improved disease treatment, and the emergence of endovascular aortic repair (EVAR) have all contributed to the fast shift in AAA epidemiology during the last few decades. Despite the reported lower AAA prevalence, the costs of screening remain reasonable due to the balancing of lower AAA incidence with lower perioperative death

rates and higher elderly survival. In places with a high smoking prevalence, screening will continue to contribute to lowering rAAA mortality for at least one generation and maybe beyond. It is advised to monitor AAA prevalence and, if necessary, shift screening to high-risk populations such as smokers. Due to a shortage or conflict of research in these areas, women focused screening, the threshold of ultrasound surveillance, and the effect of screening on quality of life should be examined. These modifications and enhancements will be supported by emerging data from current screening programs.(Earnshaw, J. J. & Lees, 2017). Only high-income Western countries, such as the United Kingdom and Sweden, have undertaken nationwide screening. In some nations, such as northern Italy, screening is more regional or specific(Altobelli et al., 2018). The idea of implementing a screening program for AAA is debatable, given its high cost and the current changing epidemiology of the disease. The reported reduced prevalence of AAA in Western countries in the past two decades could be explained by the reduced consumption of tobacco, the use of statins, and the increased prevalence of diabetes mellitus which in turn is considered a protective factor against AAA as it causes aortic wall stiffness that balances the proteolysis and thinning of the aortic wall in AAA. It is thought that it is worth starting such a program in countries with high tobacco consumption given that smoking is associated with a 3 to 4-fold risk of AAA development (Sprynger et al., 2019).

2.3.2. Screening in women

A review examining the impact of female gender on AAA presentation and screening revealed controversy surrounding the screening of women for AAA. The United States Preventive Services Task Force (USPSTF) recommends against screening women due to the low prevalence of the condition and the lack of evidence supporting its benefit for women. However, a study utilizing a Markov model to assess the cost-effectiveness demonstrated that

screening women is cost-effective, as the low prevalence is balanced by the high rupture rate. The protective effect of estrogen hormone in women against AAA pathophysiology is thought to be due the reduction of macrophage MMP production, which stops collagen destruction in the aortic wall. This is in contrast to the direct effect of androgens in men, which contributes to AAA formation; this somehow justifies the low prevalence among women when compared to men. Despite the low prevalence, women with AAA tend to have a more aggressive growth and rupture rate than men, leading to worse consequences and repair complications (Lo & Schermerhorn, 2016).

Given the exclusion of women from existing screening programs due to the reported low prevalence, and since screening is considered viable economically only when the prevalence is greater than 1%. A study was conducted to determine the prevalence of AAA, associated risk factors, and high-risk groups among 50,000 women. A prevalence of 1.57% was found among women with advanced age (> 65 years), smoking, hypertension, and a history of cardiovascular disease identified as risk factors. Women with a history of smoking, peripheral vascular disease (ABPI ratio < 0.9), and > 50% stenosis of the carotid artery had the highest prevalence, suggesting the need for targeted screening in this subgroup. (Chabok et al., 2016) While women have been excluded from current screening programs due to the low prevalence of AAA, recent economic analysis has shown that AAA screening in men will remain cost-effective even at very low prevalence rates like those observed among women. (Benson et al., 2018) In the first assessment of the long-term benefits, harms, and cost-effectiveness of screening women aged 65 or older, a simulation model incorporating available data from systemic reviews, trials and registries was utilized. The results indicated that applying a screening program for women in a way similar to that applied for men in the UK is not cost-effective, with an ICER of 30000 £/ QALY, 33% overdiagnosis rate, and a reduction in AAA-related mortality by 3% in women aged 65-95 years. However, modifications to screening such

as starting the screening at the age 70 years instead of 65, considering an aortic diameter measurement of 2.5 cm as aneurysmal instead of 3 cm, and lowering the cut-off point of repair from 5.5 cm to 5 cm, have been shown to be cost-effective, with an ICER of 23000/QALY, with a rate of 55% overdiagnosis, detection a larger number of AAA in 1.2% of the screened population, and 8% reduction in AAA- related mortality among 70-95 years women (Sweeting et al., 2018).

2.3.3. screening during echocardiography

Since heart disease and AAA share common risk factors, several studies have assessed opportunistic screening of patients >65 years old for AAA during transthoracic echocardiography (TTE) and reported that it is highly feasible, reliable, and effective. This required no additional equipment; the aorta was easily visualized in 95% of cases and lengthened the echocardiography examination time by a maximum of 3 minutes and by 5 minutes if a AAA was detected. The reported AAA prevalence among the scanned groups ranged from 3.7% to 8.7%. (Schwartz, Rashkow & Akella, 1996). A systemic review and meta-analysis were conducted on opportunistic screening for AAA during transthoracic echocardiography in which data from 20 observational studies was analyzed. It was reported that the pooled prevalence of AAA was 3.3% in the entire population, 4.6% in men, and 1.4% in women with the mean age being between 66-85. These figures are comparable to those published by early randomized control studies such as MASS, and contrary to current screening programs, such data suggests that AAA is more prevalent in people with cardiac illness. The authors concluded that this focused screening technique is advantageous and should be investigated in countries where there are no national screening programs or where national screening programs are no longer cost-efficient owing to changing disease epidemiology (Argyriou et al., 2018).

2.3.4. Targeted screening

Most national screening programs for AAA are focused on men aged 65 years or older, which may fail to identify AAA risk in other groups, including women and younger men. To address this issue, the effectiveness of three alternative screening strategies targeting high-risk individuals based on their cardiovascular disease (CVD) risk has been evaluated, including those undergoing coronary angiography, peripheral arterial disease (PAD) assessment, and community-based CVD risk event assessment. The results indicated that AAA prevalence was higher in the CVD group, suggesting that targeted screening based on the risk of CVD could be a viable alternative approach when national screening programs are not available. Targeting other risk factors, such as smoking status or family history, was not recommended as it would either add no additional value or miss many AAA. This CVD- based targeted approach has the advantage of providing access to those of AAA risk and are often excluded from screening programs, such as women and younger men, and can be built on existing pathways of health care (Jones et al., 2016). After reviewing current studies, the question of whether shifting to more targeted AAA screening criteria would be more effective in increasing the detection of AAA was raised. This is because almost half of individuals with AAA do not meet the current inclusion criteria for screening programs, and existing knowledge lacks a global truth on AAA, as its incidence varies among ethnic groups due to differences in cardiovascular risk factors. Therefore, a more target approach based on CVD risk may be a more effective strategy for identifying AAA risk in individuals who are currently excluded from screening programs (Spanos, Labropoulos & Giannoukas, 2018).

2.3.5. Worldwide variability of screening programs

In 2013, a report was published that assessed the state and the variations in AAA screening programs in Western countries. The report collected data on the state of the screening program,

the inclusion criteria of participants, the measurements and definition of aortic aneurysms, and the surveillance intervals. At the time of publication, national screening programs were implemented in six countries: the USA, England, Scotland, Wales, Sweden, and North Ireland, with a screening trial ongoing in Italy. The majority of screening programs included men aged 65 years old or older, with the exception of the USA, New Zealand, and Italy, where women were also included. Screening in the USA was limited to those who ever smoked, while New Zealand screened high-risk individuals for cardiovascular disease. An aortic diameter of 3 cm or more is considered aneurysmal, and surveillance intervals vary greatly between countries and systems, primarily related to the size of the aneurysm. Several barriers were identified against the introduction of national screening programs, including cost, sonographers' training, database development, and the geographic distribution of sonographers. The authors recommended the continuous publication of data on AAA screening programs to add them to the existing knowledge and help other countries establish their own screening programs (Stather et al., 2013).

Developing countries are encouraged to initiate epidemiologic research on AAA due to the increased life expectancy of the population and the preventable mortality from AAA. This could be implemented by using portable ultrasound devices to scan the aorta as a part of the physical examination in the first outpatient clinic visit, providing an easy, reliable, and cost-effective method of screening for AAA. (Munoz-Mendoza, Jerson|Pinto Miranda, Veronica A.|Quevedo, Henry C.|Hebert, Kathy, 2013).Controversies exist regarding the selection of the population to be screened in national screening programs, particularly the controversial screening of women, which requires further trials, especially for those at high risk: smokers and those with a family history of aortic diseases. With the changing epidemiology of AAA, which is becoming less prevalent, some recommend screening men at older ages rather than at 65 years (Kostun & Malik, 2016) .

The proper method of AAA maximum diameter measurement has no universal consensus, with the inner-to-inner (ITI) wall measurement used in UK's NAAASP, the leading edge to the leading edge (LELE) method used in the Swedish screening program, and the outer-to-outer (OTO) method used in the small AAA trial (Figure 2.2). This variability in measurement methods results in variation in the estimated prevalence, either by over or underestimating it, depending on the method of measurement (Earnshaw, J. J. & Lees, 2017). Table 2.1 summarizes the features of current AAA screening programs worldwide (Benson et al., 2018).

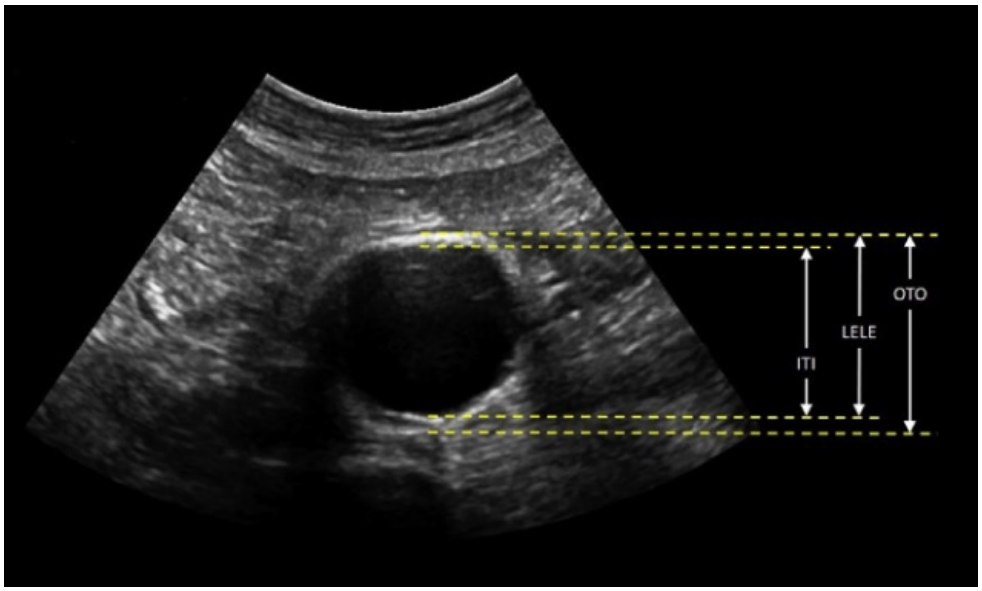


Figure 2. 2 *Caliper placement for measurement of aortic diameter. Abbreviations: ITI: inner to inner; LELE: leading edge to leading edge; OTO: outer to outer.* (Wanhainen et al., 2019)

Program	Patients	Method	Threshold of inclusion into surveillance	Surveillance schedule	Referral to surgeon
UK NAAASP	Men 65th year	Ultrasound ITI	3 cm	3 - 4.4 cm yearly 4.5 - 5.4 cm 3moths	5.5 cm
Sweden	Men 65th year	Ultrasound LELE	3 cm (2.5-2.9cm rescreened at 5 years)	2.5–2.9 cm 5 years 3.0–3.9 cm 2 years 4.0–4.4 cm 1 year 4.5–5.0 cm 6 months 5.0–5.4 cm 3 months	5.5 cm
USA	Men 65–75 years Women with significant family history	Ultrasound Not specified	3 cm	2.9–2.9 cm 5 years 3.0–3.4 cm 3 years 3.5–4.4 cm 12 months 4.5–5.4 cm6 months	5 cm

Table 2. 1 *Variabilities between current screening programs worldwide. Abbreviations: ITI, inner-to-inner measurement; LELE, leading edge-to-leading edge; NAAASP, national abdominal aortic aneurysm screening program*.

2.3.6. AAA screening in Saudi Arabia

In 1991, a screening study was carried out at King Abdul-Aziz University Hospital, Jeddah City, western Saudi Arabia. The study recruited 392 patients aged between 60 and 80 years old

over a period of 18 months during their visits to the investigator's outpatient clinic or when accompanying their relatives to the same primary health care center. The patients were categorized into three groups: the control group, the hypertensive group, and the peripheral vascular disease group. Demographic and risk factors information were obtained, and systolic blood pressure measurement, clinical examination, ankle brachial pressure index examination, and an ultrasound scanning of the abdominal aorta with measurements taken at three levels were performed on all patients. The study detected seven AAA cases in all groups, indicating an overall prevalence rate of 7%, 1%, and 0.5% in the peripheral vascular disease group, hypertensive group, and control group, respectively. The study showed evidence of a higher ultrasound detection sensitivity of AAA (98%) compared to clinical examination (42%). Based on the results, the author concluded that screening the elderly population with peripheral vascular disease for AAA is highly recommended (Al Zahrani et al., 1996).

In a retrospective study, 2032 abdomen CT of male patients aged 65-75 years were reviewed from the Picture Archiving and Communication System (PACS) with the period January 2011 to December 2016 to investigate the incidence of AAA. The study identified a total of 6 cases of AAA, yielding a low incidence rate of 0.3%. given the limited setting of the study, conducted solely in a tertiary hospital that receives referrals, and the absence of some risk factors among the study population, the authors recommend a pilot screening program for this demographic. Such a program could provide more comprehensive insights into the prevalence of AAA and enable early detection and treatment. (Alomran et al., 2018).

2.4 AAA repair

2.4.1. UK Small Aneurysm Trial

The UK Small Aneurysm Trial (UKSAT) was a significant study carried out to assess the most effective strategy for managing small abdominal aortic aneurysms (AAAs). The study, which was conducted in the United Kingdom, aimed to determine whether early surgical repair or an extensive ultrasound monitoring strategy would result in better results for patients with small AAAs. The research included 1090 participants aged 60 to 76 years with aneurysms ranging from 4.0 to 5.5 centimeters in diameter randomized into two groups: an elective early open surgery group and an ultrasound surveillance group and monitored them over several years. The findings of the UKSAT yielded vital information about the normal progression of small AAAs, aiding in the formulation of clinical judgments, and enhancing the quality of patient treatment. (The U.K. Small Aneurysm Trial: design, methods, and progress. The UK Small Aneurysm Trial participants. 1995). A 6-year follow-up for survival indicated a significant similarity of 64% in both groups. This finding can be attributed to a higher-than-expected mortality rate during elective surgery, which compensates for a minor reduction in the risk of rupture and mortality rates found later in the surgical group. (United Kingdom Small Aneurysm et al., 2002). 8 years follow-up showed that the early surgery group had better long-term survival rates (36·1 percent) compared to the ultrasound surveillance group (32·7 percent). (United Kingdom Small Aneurysm et al., 2002) However, longer-term follow-up after 12 years, indicated a mortality rate in the repair group of 63.9% while in the surveillance group, it was 67.3%. concluding that there are no long-term benefits of early elective open repair of small aneurysms (Powell, 2007).

2.4.2. Endovascular Repair (EVAR) Trial 1

The primary objective of the EVAR trial 1 was to assess the efficacy and safety of endovascular interventions in the management of aortic aneurysms. This trial sought to evaluate the results and advantages of utilizing minimally invasive methods for the treatment of aortic aneurysms through the utilization of endovascular stent grafts. This novel approach avoids the necessity for traditional open surgery and instead involves the insertion of a catheter through a small incision, facilitating the placement of the stent graft in the affected region. The EVAR study 1 recruited a total of 1252 participants from 37 locations in the United Kingdom throughout the period from September 1, 1999, to August 31, 2004. Patients were required to be 60 years of age or older, have aneurysms with a minimum diameter of 5·5 cm (evaluated by CT), and be considered appropriate and physically capable for either EVAR or open repair. (Cronenwett, 2005) Between 0- and 6-months following randomization, patients in the EVAR group had a decreased mortality rate. Endovascular aneurysm repair (EVAR) has an initial advantage in terms of survival, which diminishes progressively over time. However, after 3 years, there is a return in death rates (Lederle et al., 2009). and over a follow-up period of 8 years or more, open repair demonstrated a considerably reduced mortality rate. The comparatively lower long-term survival of EVAR in comparison to open repair require the necessity for continuous monitoring of EVAR and subsequent intervention if required. The incidence of rupture following aneurysm repair was notably greater in those who had endovascular aneurysm repair (EVAR) compared to open repair. The UK EVAR trial 1 previously stated the results of the follow-up study on mortality linked to aneurysms and overall mortality, which extended up to a duration of 10 years. At this stage, no difference was seen between the outcomes of EVAR and open abdominal aortic aneurysm repair. Petal et al. presented an extensive study comparing the long-term outcomes of EVAR and open repair after 15 years. The study revealed that patients who

underwent EVAR had higher rates of late aneurysm-related mortality and overall mortality compared to those who had open repair. Additionally, the EVAR group had a higher rate of re-interventions at all time points, including patients who remained free from re-intervention after 2 or 5 years. (Patel and colleagues, 2016).

2.4.3. Endovascular Repair (EVAR) Trial 2

The EVAR 2 trial intended to assess long-term total and aneurysm-related mortality in physically weak patients with abdominal aortic aneurysm (AAA) who were randomly assigned to either early endovascular aneurysm repair (EVAR) or no intervention. EVAR-2 stands as the only randomized experiment that has been able to determine if EVAR reduces mortality in patients who are physically unable to undergo open surgery. From September 1999 to August 2004, a total of 404 patients aged ≥60 years with an abdominal aortic aneurysm (AAA) diameter >5.5 cm were randomly assigned in a 1:1 ratio to two groups. One group received endovascular aneurysm repair (EVAR) (n=197 patients), while the other group received no intervention (n=207 patients) (EVAR, 2005). The 30-day mortality rate among patients who underwent endovascular aneurysm repair (EVAR) was 7.3%, whereas the initial state risk of aneurysm rupture in the group that did not receive any intervention was 12.4%. After a period of 12 years, the estimated survival rate was 5.3% in the EVAR group and 8.5% in the group that did not get any intervention. There was no difference in life expectancy between the two groups. Nevertheless, the EVAR group had a notably reduced death rate associated with aneurysms in comparison to the group that did not receive any intervention. Ultimately, EVAR had substantial long-term advantages compared to no intervention in relation to mortality caused by aneurysms, however it did not impact overall mortality. (Sweeting et al., 2017).

2.5 Shear wave elastography of aorta

Shear wave elastography (SWE) is a non-invasive imaging method that quantifies tissue stiffness by analyzing the propagation of shear waves through biological tissue (Chen, 2017; Schaafs et al., 2019). SWE has been the subject of numerous investigations that have evaluated the feasibility, reproducibility, and accuracy of measuring tissue stiffness and detecting alterations in stiffness associated with specific diseases in different organs, including the liver, breast, thyroid, and blood vessels. Figures 2.3 to 2.7 illustrate the different uses of SWE in various body organs.

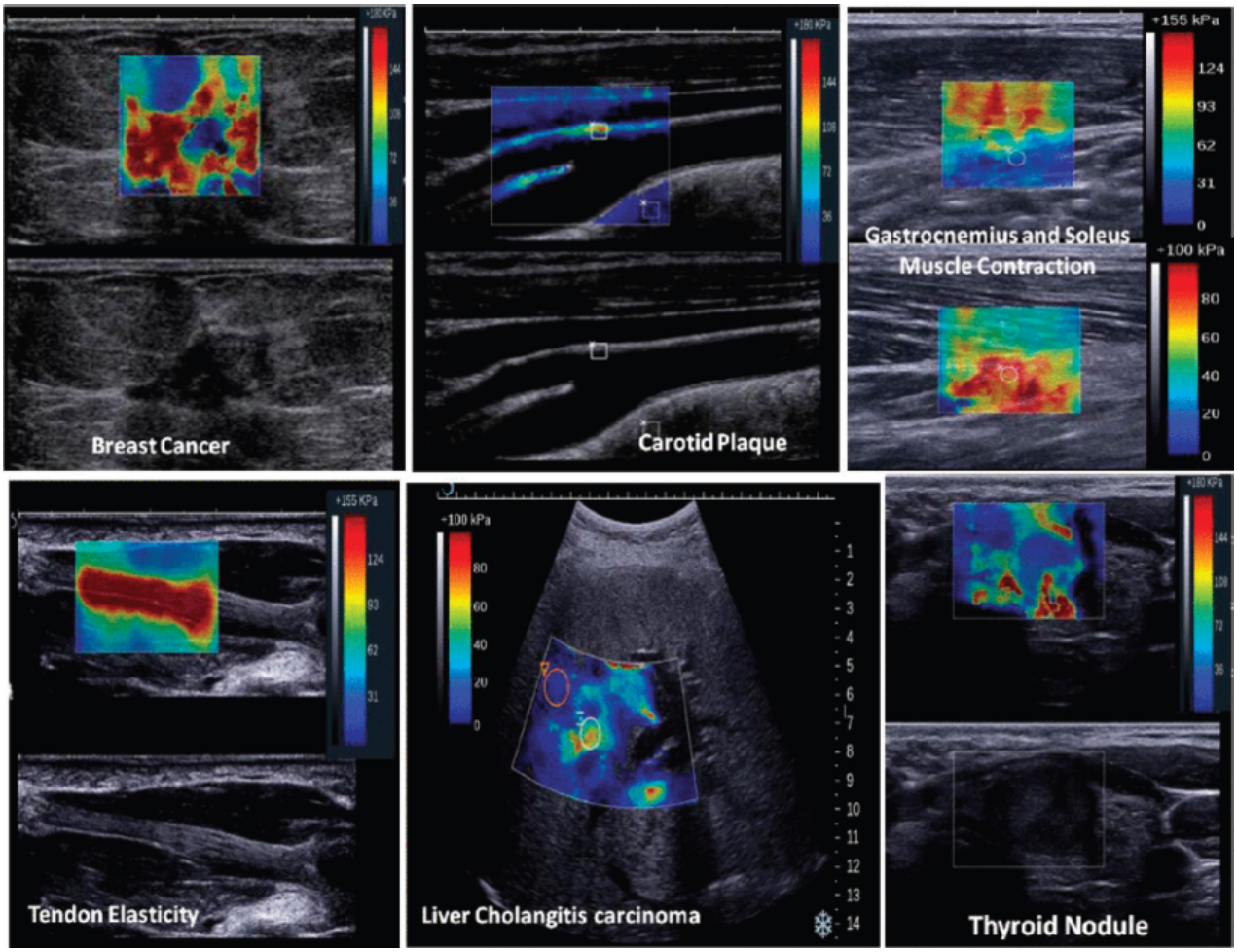


Figure 2. 3 *Clinical examples of shear wave elastography.* *(Tanter & Fink, 2014)*

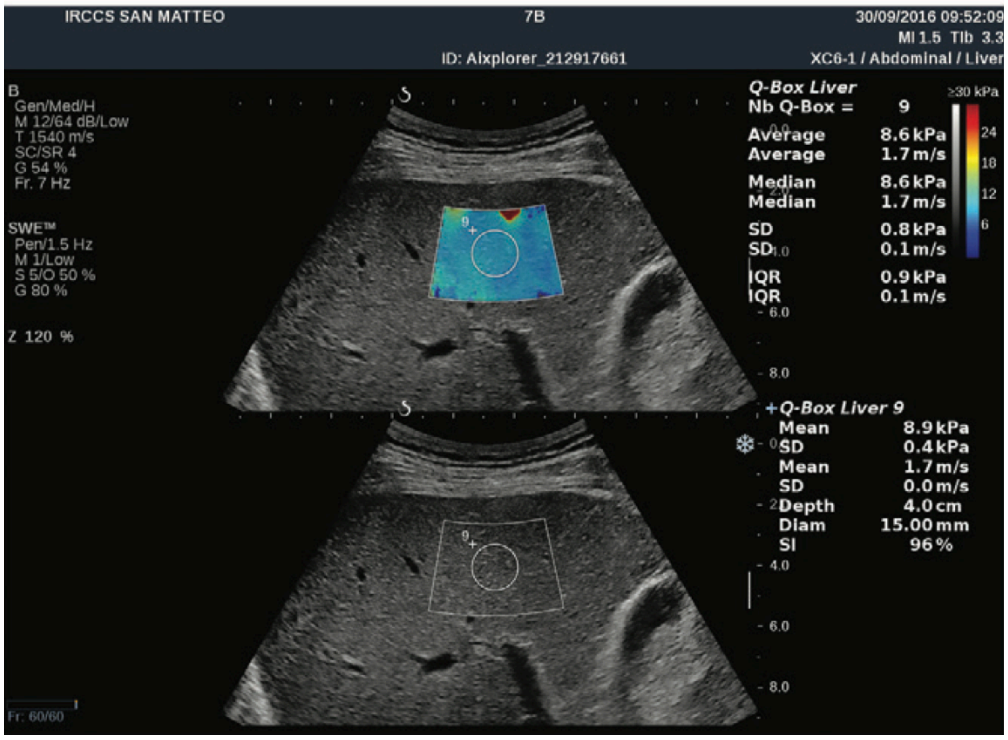


Figure 2. 4 *Liver images obtained with 2D SWE (SSI; Supersonic, Aix-en-Provence, France). The stability index (SI) is an indicator of temporal stability, and it is displayed while positioning the measurement box (Q-Box). An acquisition of good quality should have a stability index greater than 90%. Top image is velocity map, and bottom image is B-mode image.* (Barr et al., 2020)

Table 1 ShearWave™ Elastography: qualitative classification (Qual).

Types	1	2	3	4	5
Homogeneity	Homogeneous	Not very homogeneous	Heterogeneous	Heterogeneous	Heterogeneous
Maximum color	Blue	Green	Yellow	Red	Red
Hard area	0	0	Intra- or Perilesional	Intra- or Perilesional	Perilesional
Intralesional echo	Present	Present	Present	Present	Absent (no echo)

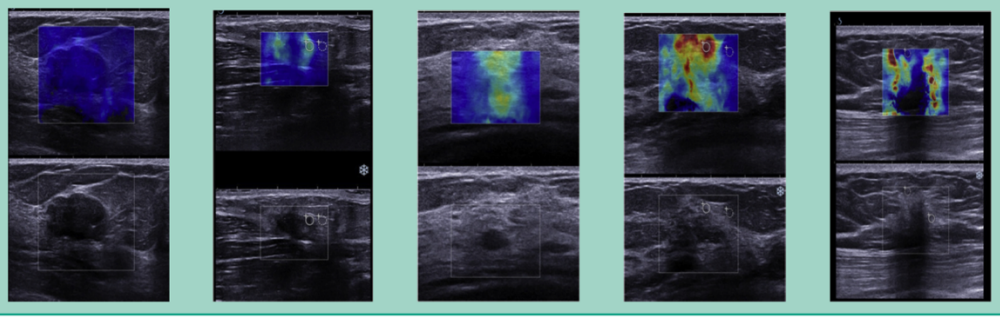


Figure 2. 5 *Shear wave elastography qualitative classification of breast lesions.* *(Klotz et al., 2014)*

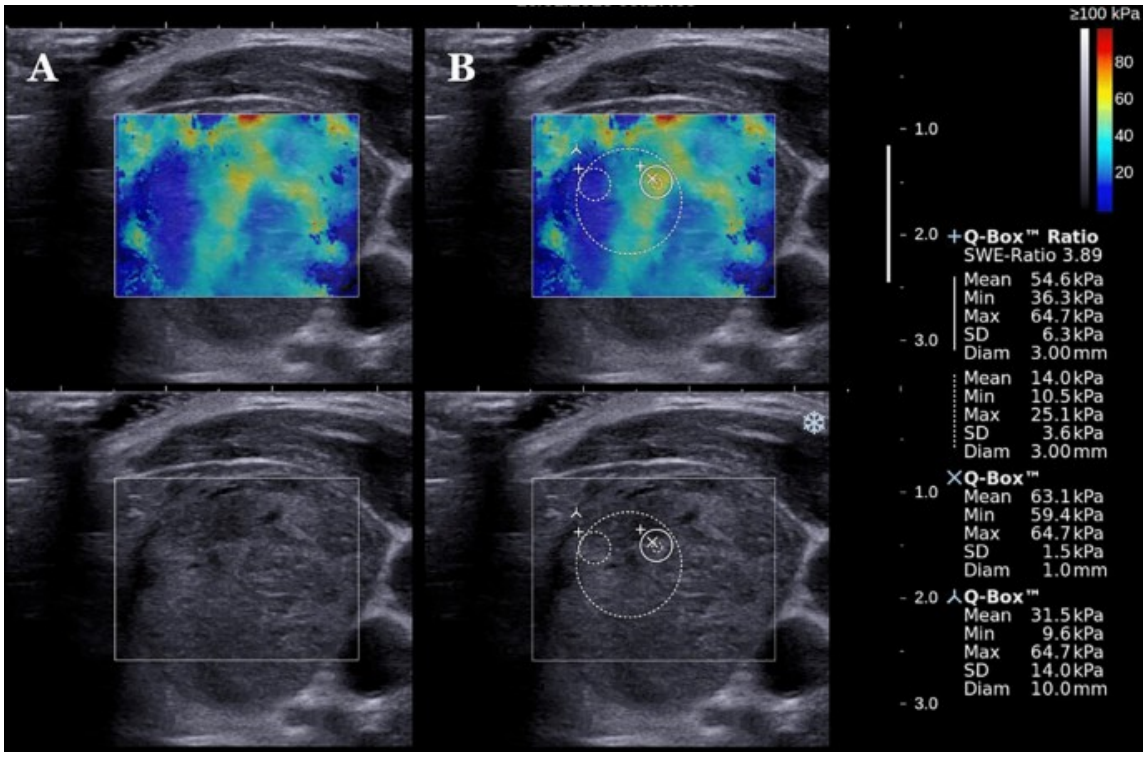


Figure 2. 6 *Thyroid nodule SWE image demonstrating the acquisition and placement of region of intrest (RIO). (A) Frozen SWE image;(B) the same SWE image with ROIs and shear wave velocity measurements on the right.* *(Swan, Nielsen & Bonnema, 2021)*

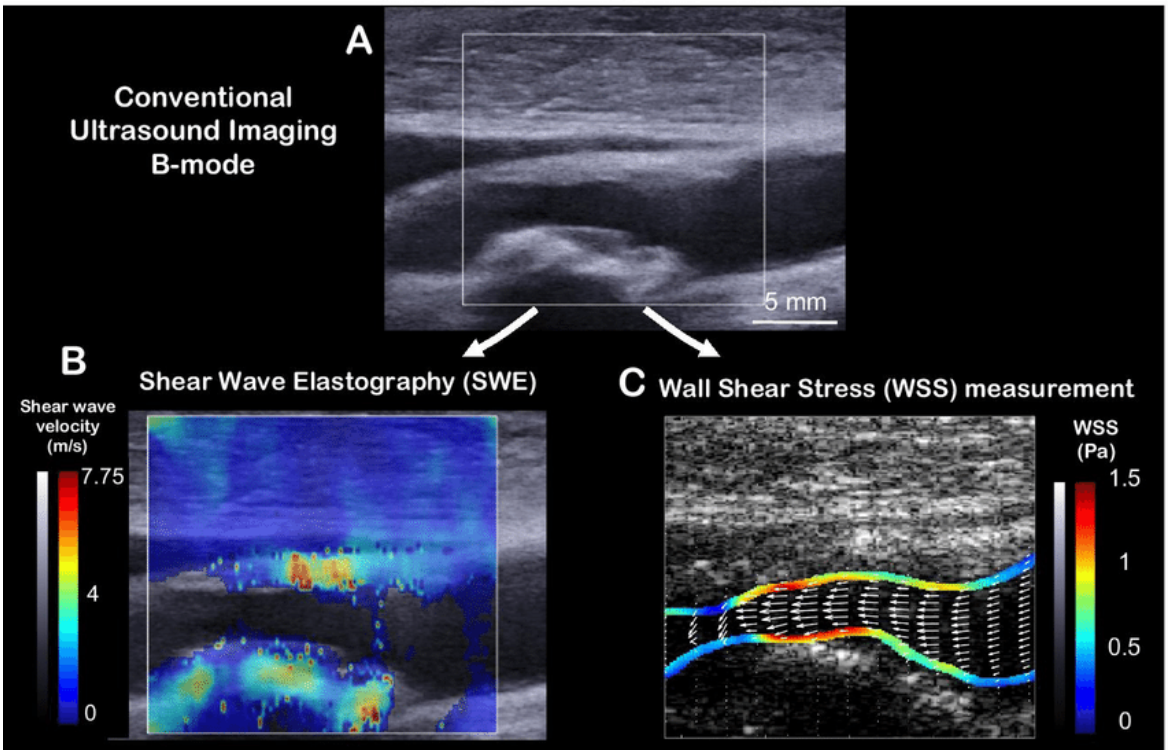


Figure 2. *7 A carotid plaque was imaged with ultrafast ultrasound using successive B-mode acquisitions (A), shear wave elastography (B), and ultrafast Doppler with Wall shear stress measurement (C).* *(Goudot et al., 2022)*

Elgeti et al. conducted the first study of its kind to evaluate the effect of smoking on aortic stiffness and reported a 12% increase in aortic stiffness in smokers compared to nonsmokers. The study indicated that these changes are detectable at an earlier stage, prior to the occurrence of morphological changes.(Elgeti et al., 2022) .SWE was utilized to assess the impact of age and hypertension on aortic stiffness and observed significantly higher values in individuals with arterial hypertension. (Schaafs et al., 2019). Multiple studies have reported the usefulness of SWE in detecting endoleaks following endovascular aneurysm repair (EVAR) (Bando et al., 2021). The first study of its kind in humans investigated the feasibility of SWE in the evaluation of the abdominal aorta post-EVAR to rule out endoleaks (Figure2.8). The study reported high sensitivity in detecting endoleaks reaching 100%, which is comparable to that of computed tomography angiography (CTA) and superior to color Doppler ultrasound (Voizard et al.,

2020b). SWE is considered a promising technique for the evaluation of the stiffness of the abdominal aorta non-invasively it has the option to provide diagnosis and management of various cardiovascular diseases.

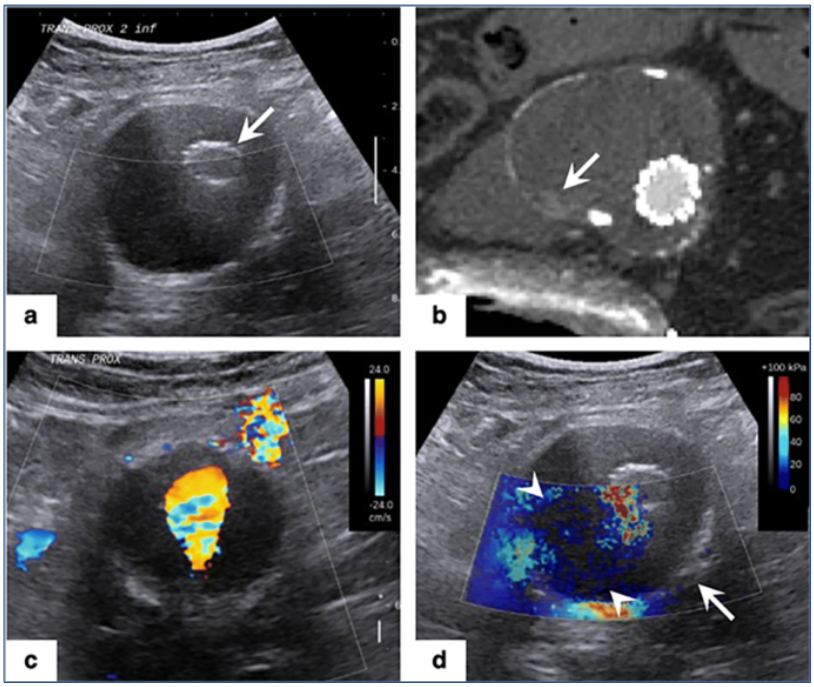


Figure 2. 8 *An endoleak (**a**) b-mode ultrasound image shows the stent graft (arrow). (**b**) Axial CTA confirms a type II endoleak (arrow) from the median sacral artery. (**c**)color ultrasound shows no signal outside the stent graft. (**d**) SWE demonstrates the absence of an elasticity signal in the right posterolateral sac (arrowheads) compatible with an endoleak. Note the absence of a signal in the left posterior sac wall indicating a non-diagnostic region (arrow).* *(Voizard et al., 2020b)*

2.6 The utilization of the Butterfly iQ probe for aortic aneurysm evaluation in screening programs

The usefulness of a handheld butterfly probe lies in its small size, portability, and low cost. These features enhance AAA early detection and management while providing easy access to the population. The butterfly probe is simple to use and requires minimal training; its simple design, straightforward controls, and ability to switch between different imaging modes (curved to linear, low-to-high-frequency), make it usable even for healthcare practitioners with limited experience in ultrasound imaging (Le et al., 2022). The portability of the butterfly probe allows screening in a range of settings, including distant or underdeveloped locations with limited access to specialized healthcare institutions. Additionally, the butterfly probe's low cost in comparison to conventional ultrasound devices makes it a financially viable alternative for mass screening programs (Baribeau et al., 2020). However, it has a few limitations. It is not designed for prolonged imaging, as continuous use (15-20 minutes) can lead to a rise in its temperature and the activation of the automatic cooling feature, freezing all imaging until the device has cooled down, leading to some potential delay in between scans. Moreover, the Image quality is slightly inferior to that of conventional ultrasound machines, but the images obtained remain adequate for diagnosis (Le et al., 2022). Despite these limitations, the advantages of the butterfly probe make it a desirable tool for population AAA screening, enhancing the feasibility of mass screening programs. The accuracy, reliability, and feasibility of the Butterfly iQ probe in aortic evaluation was compared to those of conventional ultrasound machines. It was reported that the Butterfly iQ probe is highly accurate, reliable, and feasible in the evaluation of the aorta and can be used as an alternative to standard ultrasound machines. However, further investigation of its reliability in the detection of AAA was recommended(Alfuraih et al., 2021)

CHAPTER 3. Methodology & Study Design

3.1. Introduction

This research project is divided into three parts. The first and most fundamental part is the AAA prevalence and risk factors study. The second is the Shear wave elastography study and the last, is the Butterfly iQ probe comparison study. This chapter will present in detail the materials and the precise methodology in which the three studies were carried out.

3.2. Ethical Approvals

The study protocol has been reviewed and approved by the local IRB (Institutional Review Board) ethics committees at four tertiary hospitals across Riyadh, namely:

1- King Abdullah bin Abdul-Aziz University Hospital (KAAUH) and health research centre at Princess Norah Bint Abdulrahman University (PNU).
(IRB log number: 19-017).

2- King Saud Medical City (KSMC). (IRB log number: H1RE-24-Dec19-03)

3- King Khalid University Hospital (KKUH). (IRB ref :20/D156/IRB proj No. E-20-4550)

4- National Guard health affairs (NGHA) and King Abdullah International Medical Research Centre (KAIMRC). (IRB Memo SP20. 088.R)

3.3. AAA prevalence study

3.3.1. Study Design

The study employed a cross-sectional prospective design and was conducted at multiple tertiary hospitals across Riyadh city, the capital of Saudi Arabia.

3.3.2. Participants recruitment

Participants were recruited during their scheduled visits to the general & vascular ultrasound or Eechocardiography departments for an ultrasound scan between November 2019 and April 2022. Due to Covid-19 pandemic lockdown, there was an 8-month cessation period.

3.3.3. Inclusion Criteria

The inclusion criteria for this study were as follows:

- Male and female adults, including both Saudi and non-Saudi individuals.
- Age greater than 50 years.
- Both patients with and without previously known AAA were eligible for inclusion, as the primary objective is to estimate the prevalence of AAA.

3.3.4. Exclusion Criteria

The exclusion criteria for this study were as follows:

- Adults with abdominal gases that could obscure the visualization of the abdominal aorta.
- Participants who had undergone surgical repair of AAA.
- Lack of acceptance to participate in the study.

3.3.5. Consent and questionnaire

Patients over the age of 50 who attended appointments in the ultrasound or echocardiography department were informed about the research and asked for their consent to participate.

Participants were then provided with an electronic questionnaire via REDCap (Research Electronic Data Capture) software, which included questions related to age, gender, lifestyle, and AAA risk factors (such as smoking history, hypertension, cardiovascular disease, family history, and other comorbidities). The investigator filled in the questionnaire with the participant to ensure understanding of the questions and complete answers. The questionnaire can be accessed via https://redcap.pnu.edu.sa/redcap/surveys/?s=RENHEFP8PA , A copy of the consent form is included in the appendices (appendix 1).

3.3.6. Assessment of the aortic diameter

An ultrasound duplex exam was performed to scan the abdominal aorta. In which the patients were positioned in a supine position on the examination bed and exposed their abdomen. The exam was conducted with a low-frequency curvilinear transducer (5-1,5-2 MHz) or a sector transducer (5-1 MHz) of a high-frequency ultrasound machine. The aorta was scanned from its entrance into the abdomen to its bifurcation into the right and left common iliac arteries, and diameter measurements were obtained at three levels: supra-renal, infra-renal, and just above the bifurcation (Figure 3.1). Antero-posterior (AP) diameter measurements were taken at the areas of the largest diameter on B-mode transverse and longitudinal views using the Inner to Inner (ITI) wall measurement approach (Figure 3.2a), similar to that used in the UK national AAA screening program (NAAASP) as this method of measurement is more reliable and reproducible than other methods (Hartshorne et al., 2011). Iliac arteries were also included in the scan since AAAs are commonly associated with aneurysms in iliac arteries. If an AAA was detected, the largest (ITI) AP diameter measurement was taken at two planes: transverse and longitudinal (Figure 3.3), and the Color Doppler option was used to assess the aneurysm. The severity grade of aortic calcifications and thrombosis, if present, was recorded.

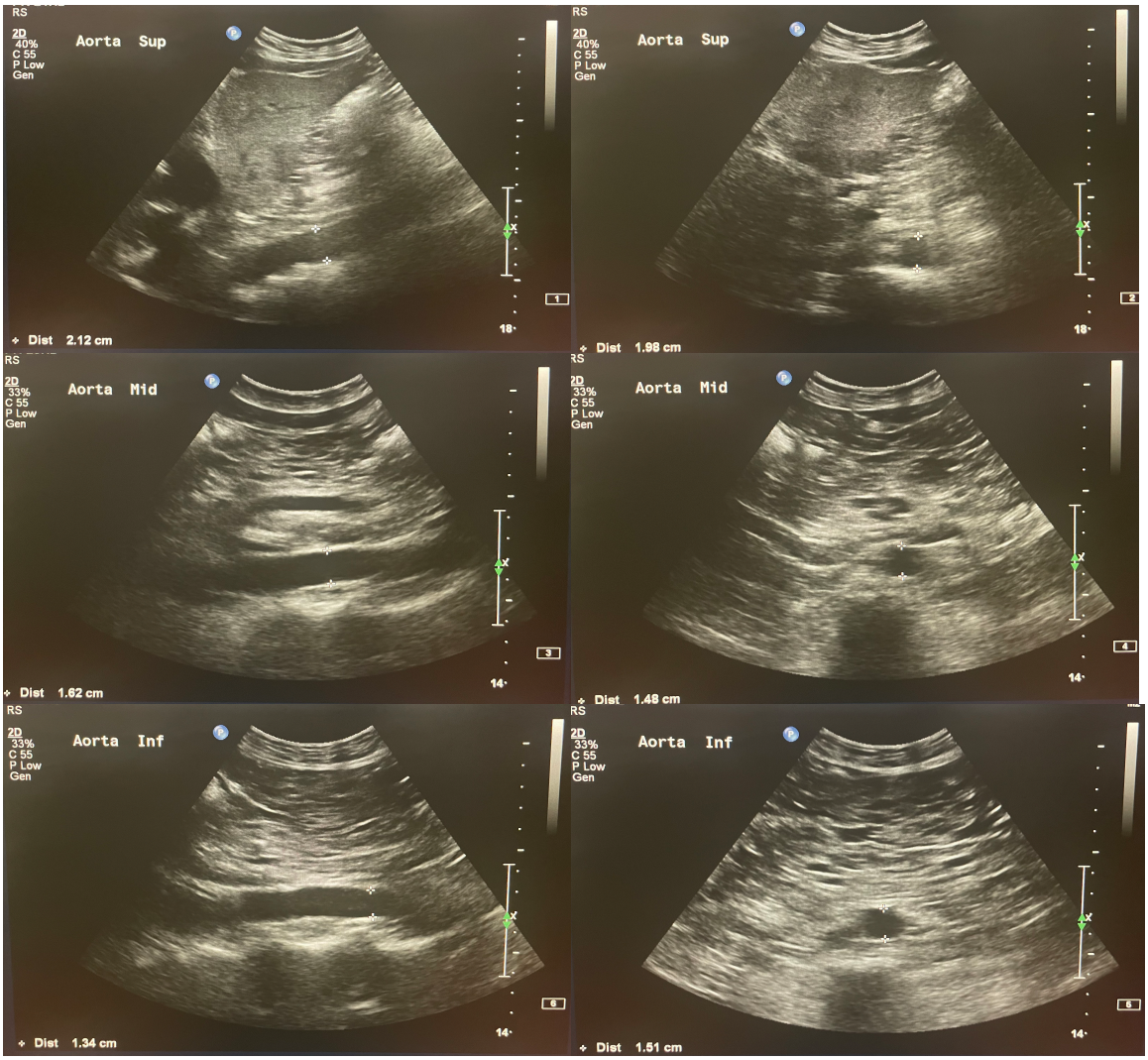


Figure 3. 1 *Aortic ultrasound of a 71-year-old patient, presenting the proximal, mid, and distal aorta in both longitudinal (right) and transverse (left) views. The ITI diameter measurements suggest a normal Aorta.*

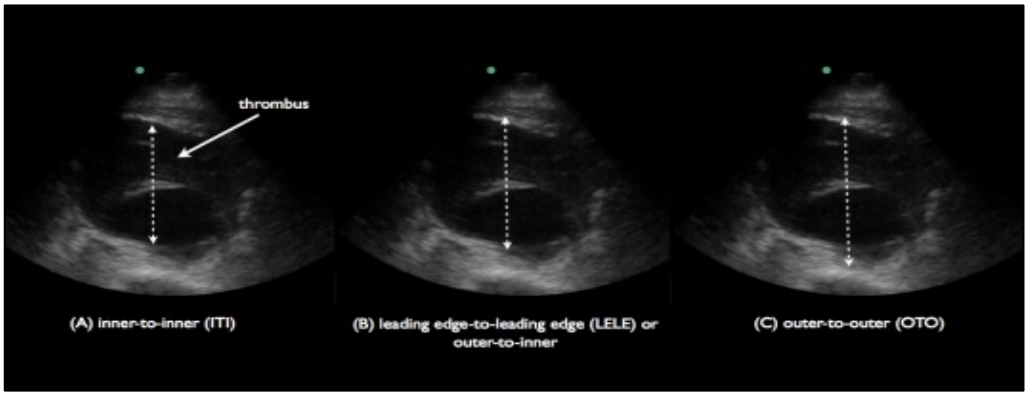


Figure 3. 2 *Axial ultrasound image of an abdominal aortic aneurysm with thrombus, demonstrating the three common methods to measure the aorta AP diameter (Lema PC et al, 2017).*

In case an AAA was detected for the first time, the radiologist was informed, and the U/S exam report included a statement indicating the size of the aneurysm and the need for referral to a vascular surgeon if the size was greater than 5.5cm due to the risk of rupture. Images were stored and measurements were recorded in the data collection section on REDCap (appendix 2). Four diameter measurements were obtained for each of the suprarenal, infrarenal, and distal aorta on a random subset of 32 participants, including patients with AAA, to assess intra-observer and interobserver diameter measurement reproducibility. The researcher obtained three diameter measurements of each section of the aorta with the probe being removed from the skin between measurements, while a second observer (competent sonographer) obtained the fourth diameter measurement being blinded to measurement readings. Patient privacy and dignity were maintained throughout the exam.

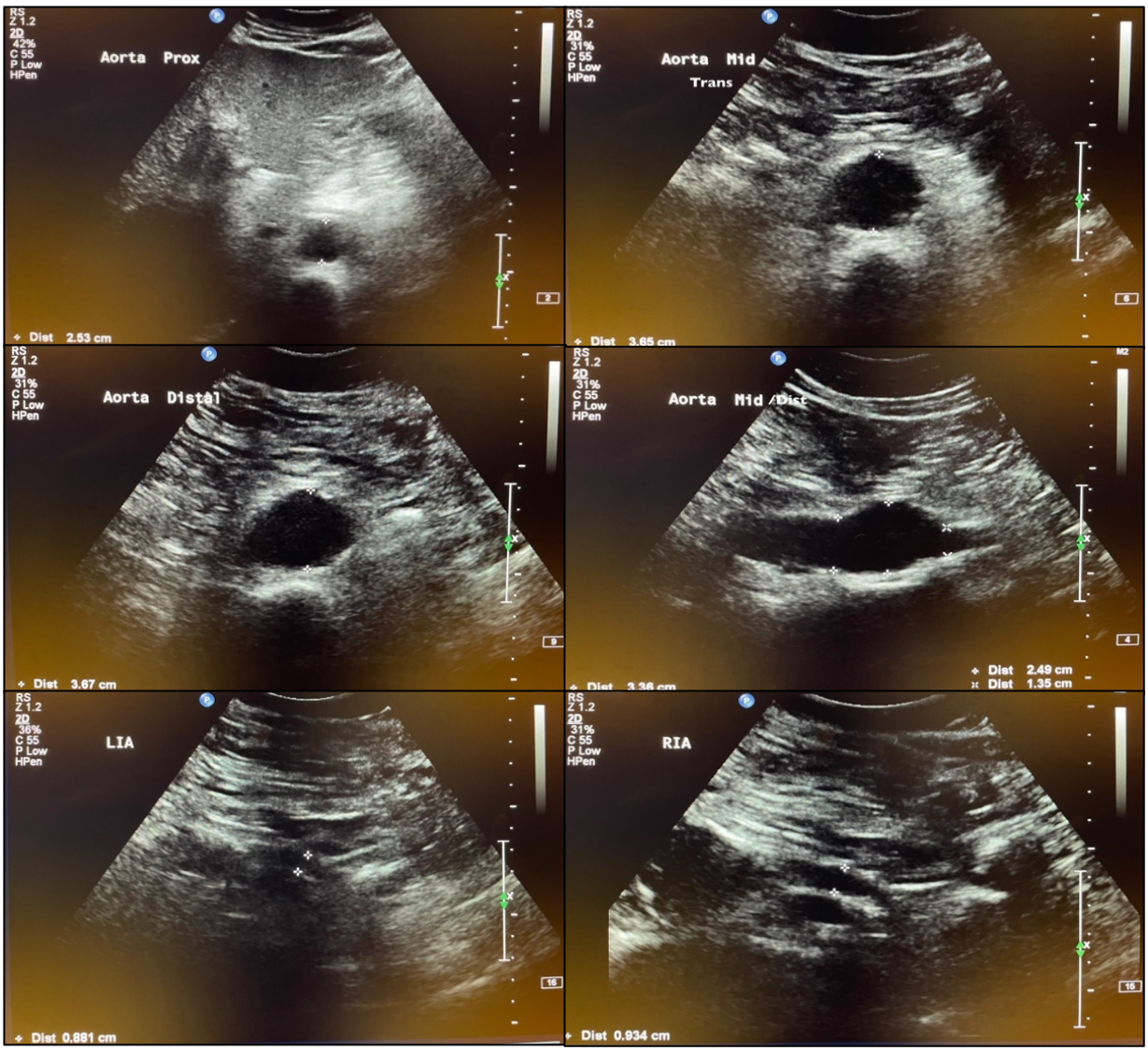


Figure 3. 3 *Aortic ultrasound of a 71-year-old patient with AAA, including the proximal, mid, and distal aorta, as well as the RT and LT iliac arteries. The ITI diameter measurements indicate the presence of AAA at the mid and distal location of Aorta.*

3.3.7. Clinical data

The medical file of each participant was accessed to collect the following data:

- Weight, height, and Blood pressure readings recorded in the nurse assessment report.
- Results from previous electrocardiograms (ECGs).

- Results from previous lab test conducted within the past six months including: lipid profile, blood sugar levels, renal function, and basic metabolic profile blood tests (refer to appendix 2 for details).

3.3.8. Power Calculations

The Determination of the appropriate sample size for the study involved seeking statistical consultations from two professionals: Ms. Toqir Mukhtar from London Research Design Service (RDS) and Dr.Omar Aldbasi from the data clinic of the Health Research Center at Princess Norah University (PNU) in Riyadh. Through their expertise, it was determined that a sample size of 680 participants would be necessary.

The sample size calculation for this study was based on the population of Riyadh city, consisting of individuals over the age of 50, which was estimated to be 610,000 according to the General Authority of Statistics in 2016. The proportion of AAA prevalence used for the sample size calculation was 1.8% based on a previously published Study regarding the screening of Abdominal aortic aneurysm in Jeddah, Western Saudi Arabia (Al Zahrani et al., 1996) . The precision or absolute error, for the sample size calculation was set at 1%.

The formula used to calculate the sample size of a quantitative variable is as follows (Charan & Biswas, 2013):

Sample size = $(Z_{i-\alpha}^2\, p\, (1-p)) / d^2$

Where:

- **Z** represents the statistic for a level of confidence, with a conventional value of 1.96 for a 95% confidence interval with 5% Type 1 error and a P value of less than 0.05.
- **P** represent the expected proportion in the population based on the previous studies.
- **d** represents the absolute error precision, which must be decided by the researcher.

By substituting the corresponding values into the formula, the sample size was calculated as follows:

Sample size = $(1.96^2 * 0.018(1 - 0.018))/0.01^2$

Sample size = 680

3.3.9. Outcome Measures

- Abdominal aorta diameter measured using an Inner to Inner (ITI) wall measurement approach, at three levels: suprarenal, infrarenal and above the bifurcation.
- Demographic and lifestyle information of the participants.
- Result from electrocardiogram (ECG) test conduction on the participants.
- Results from the participants' laboratory tests.

3.4. Shear wave study

3.4.1. Study Design

The study design employed in this research is a small prospective analytical study, which was conducted at the vascular lab located at Hammersmith hospital, Imperial College London.

3.4.2. Participants recruitment

For this study, Participants were recruited during their visit to the vascular lab for a vascular ultrasound scan, with a total of 100 participants being enrolled. Among these, 50 were assigned

to a group comprising patients with AAA, whereas 50 were assigned to the control group. Control group did not have any clinical or diagnostic evidence of aortic aneurysm.

3.4.3. Inclusion Criteria

The inclusion criteria for this study were as follows:

- For the AAA group: Male adults diagnosed with AAA.
- For the control group: Male adults without AAA who were matched for age with the AAA group.

3.4.4. Exclusion Criteria

The exclusion criteria for this study were as follows:

- The presence of abdominal gases that could obscure the visualization of the abdominal aorta.
- Participants who had undergone surgical repair for AAA.
- Lack of acceptance to participate in the study.

3.4.5. Shear wave aortic assessment

The study obtained consent from participants for their involvement in addition to information about demographics, smoking status, and other comorbidities. The patients were then asked to lie on the examination bed and expose their abdomen for examination in a supine position, using a low-frequency curvilinear probe (5-1 MHz) of Philips IU-22 Ultrasound machine.

Patient privacy and dignity were maintained throughout the exam. The shear wave propagation speed was measured at the posterior wall of the aorta in Kilo Pascals (kPa) and multiple images were obtained (Figure 3.4). Consent, demographic information, and measurements were recorded in the data collection sheet of the SWE project on REDCap (refer to appendix 3).

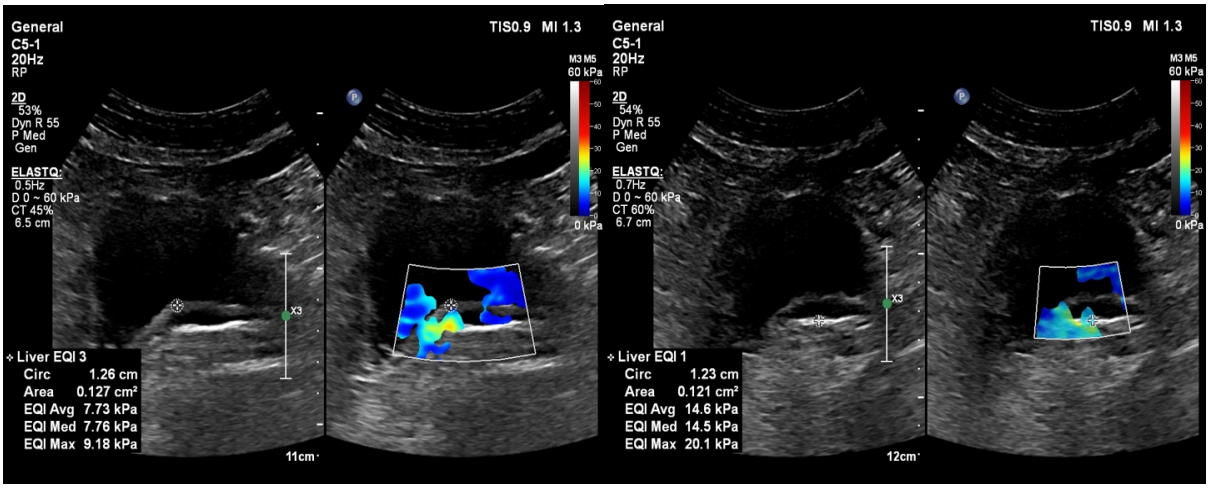


Figure 3. 4 *Transverse ultrasound images of the aorta, demonstrating the measurement of the SW propagation speed at the posterior wall.*

3.5. Butterfly iQ study

3.5.1. Study Design

The study design employed in this research is a small prospective analytical study, that took place in the general ultrasound department of National Guard Health Affairs (NGHA) in Riyadh, Saudi Arabia.

3.5.2. Participants' recruitment

The recruitment of participants for this study involved a search in the Change Health Care (CHC) radiology solutions system using “AAA” as the search keyword. The resulting AAA cases were further filtered by date, limited to those who were diagnosed between October 2019 to October 2022. A total of fifty-one patients were initially identified as having AAA, but further review of the cases in the Health Information System: BESTCare resulted in a decrease in the number cases of AAA that could be scanned to twenty-seven, as twelve AAA patients undergone repair and the other eleven had passed away. The remaining twenty-eight participants were contacted, and a brief explanation of the research idea was provided to them. They were invited to visit the general ultrasound department for a scan. Thirteen attended their assigned appointments, while eight refused to participate. The remaining seven either didn’t answer our calls or had an out-of-service contact number.

3.5.3. Consent and Duplex Ultrasound

The researcher obtained consent from the participants for their involvement, along with information regarding their demographics, smoking status, and other comorbidities such: hypertension, diabetes mellites and hypercholesteremia. Participants were asked to lie on the examination bed and expose their abdomen. They were examined in a supine position using two probes by two operators. First, a low-frequency curvilinear probe (5-1 MHz) of EPIC 7 conventional ultrasound machine (*Philips Medical Systems.* 2019) was used to assess the aorta (Figure 3.5). The aorta was scanned through its entire length and aortic diameter measurements were obtained at two sites: the proximal aorta (suprarenal) and distal aorta(infrarenal). Three Inner-to-Inner (ITI) anteroposterior (AP) measurements and one Outer-to-Outer (OTO)

measurement were obtained at the maximum aortic width in two planes (transverse and sagittal) for each site, with the probe being removed from the skin in between measurements, ultrasound images of measurements were stored on the machine. Second, the Butterfly iQ probe (*Butterfly Network Inc.* 2018) was connected to an 8.3-inch iPad mini 6 (Apple, 2021) and used to assess the aortic diameter using the same protocol (Figure 3.6). Once the first operator (primary investigator) had finished scanning, the second operator (competent sonographer) repeated the same steps and scanned the participant using the two probes. Throughout the examination, patient privacy and dignity were maintained. Several images were obtained by the two operators (Figure 3.7). Consent, demographic data, and measurements were recorded in the data collection sheet of the Butterfly iQ project on REDCap (refer to Appendix 4).



Figure 3. 5 *EPIC 7 ultrasound*



Figure 3. 6 *Butterfly iQ portable probe*

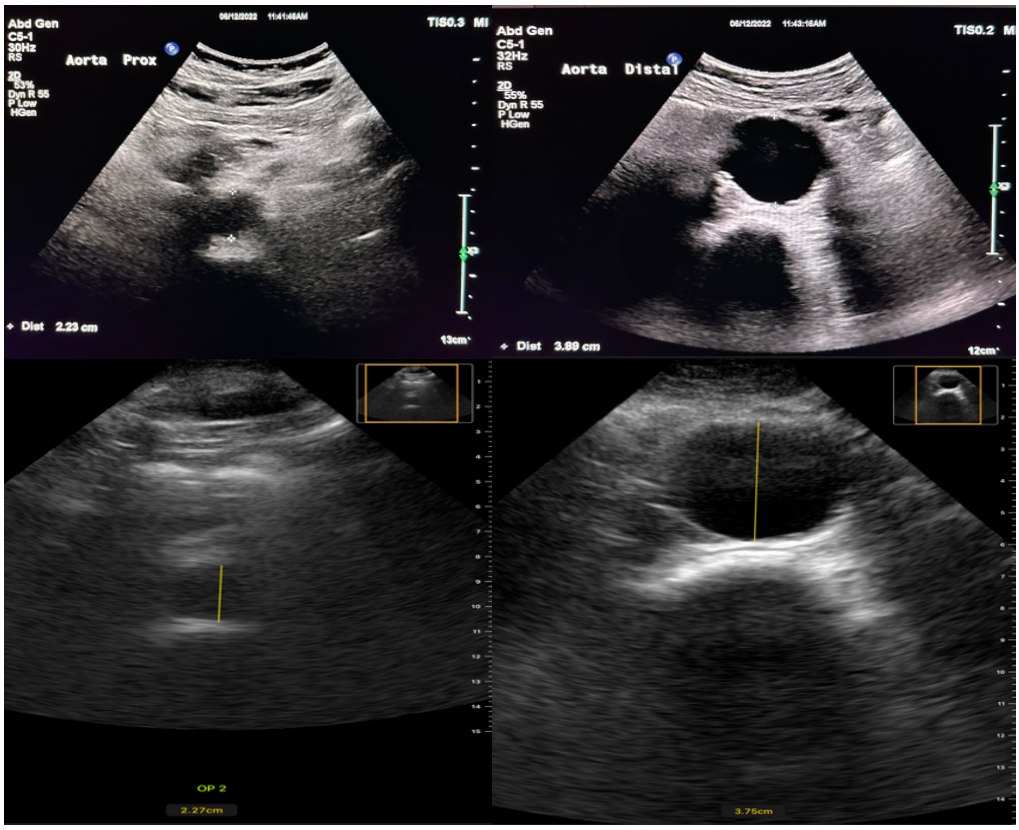


Figure 3. *7 Transverse ultrasound views of the proximal and distal aorta obtained using both the conventional ultrasound machine (top) and the Butterfly iQ probe (bottom).*

3.6. Study design

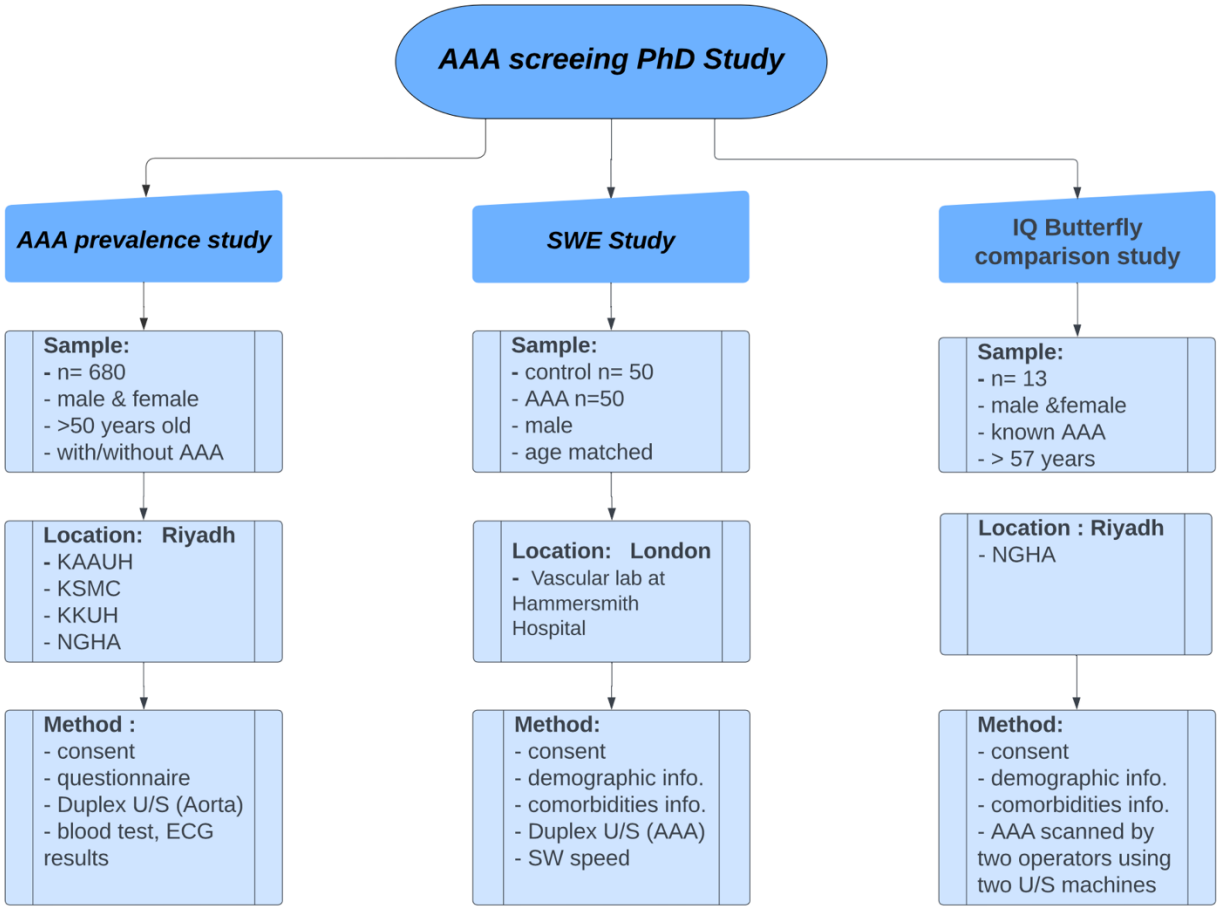


Figure 3. 8 *flow chart of the study design*

3.7. Data Management

The study utilized REDCap electronic tools, which were hosted at Princess Norah Bint Abdulrahman University (PNU), for the collection and management of the study data, including the questionnaire and data collection sheets (PA Harris, R Taylor, BL Minor, V Elliott, M Fernandez, L O'Neal, L McLeod, G Delacqua, F Delacqua, J Kirby, SN Duda,

REDCap Consortium, 2019; PA Harris, R Taylor, R Thielke, J Payne, N Gonzalez, JG. Conde, 2009). REDCap (Research Electronic Data Capture) is a secure web-based software platform designed to support data capture for research studies providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and exports procedures; 3) automated export procedures for seamless data downloads to common statistical packages; 4) procedures for data integration and interoperability with external source.

3.8. Data analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software (IBM Corp., 2017) and STATA software (StataCorp, 2021).

The first analysis of the study involved calculating the prevalence of AAA and estimating its corresponding confidence interval (CI) using the exact binomial method. Fisher's exact test was utilized to examine the association between various risk factors and the presence of AAA. This test was preferred over the Chi-square test, which is typically used for this type of data due to the small number of AAA cases. A possible second stage of the investigation would be to conduct a multivariable analysis of the risk factors and AAA (for example, using multiple logistic regression). Given the small number of AAA cases, there was not sufficient data to perform this method of analysis. Furthermore, the age distributions of patients with and without AAA were compared using an unpaired t-test. Interclass correlation coefficients (ICCs) were calculated to assess intra-observer and interobserver agreement and reliability and Bland-Altman plots were generated using Microsoft Excel to visualize the differences in mean measurements and the upper and lower limits of agreement.

The second analysis of the study compromised several steps. Firstly, the separate association between each risk factor and the occurrence of AAA was examined using logistic regression, given the binary nature of the outcome (AAA case or Control). The subsequent stage of

analysis investigated the joint association between the risk factors and AAA in a multivariable analysis, where only factors exhibiting some evidence of association with the outcome ($p<0.1$) from the initial analysis were included to reduce the number of variables. The final model was obtained via a backward selection procedure whereby non-significant variables were omitted until all remaining factors exhibited a significant association with the outcome. Odds ratios were used to represent the size of the association between each factor and case/control status, along with corresponding confidence intervals. Finally, a comparative analysis of the SWE values between cases and controls was conducted using the unpaired t-test.

The third analysis of the study evaluated the intra- and inter-observer agreement using two methods: the Bland-Altman limits of agreement method and the intra-class correlation (ICC) method. The Bland-Altman method was used to measure the size of differences between pairs of values that are likely to occur and calculate the 95% limits of agreement. Intra-observer agreement was assessed using measurements 1 and 2 only, whereas the inter-observer agreement was performed first using measurement 1 only, and then by calculating the mean of the three measurements. The ICC method was used to calculate the ratio of the between-patient variation over the total variation and assess within-patient variability. All three measurements from each observer were included in the intra-observer agreement, while the inter-observer agreement analysis used the first measurement from each observer, and then the mean of the three measurements.

CHAPTER 4: Results

This chapter will provide a comprehensive presentation and interpretation of the findings obtained from three distinct studies conducted as part of this research endeavor. Specifically, it will analyze the prevalence of abdominal aortic aneurysms (AAA) within Riyadh population, the associated risk factors, as well the efficacy and dependability of the hand-held butterfly iQ probe in the detection and evaluation of aortic aneurysms. Furthermore, this chapter will present in detail the observed differences in elasticity of the wall of the aorta between aneurysmal and non-aneurysmal aortas, thereby making a valuable contribution to the existing literature on this subject matter.

4.1 AAA prevalence study

A prospective cross-sectional screening was conducted, wherein participants underwent ultrasound scanning to determine the presence of AAA. In addition, participants responded to a questionnaire to collect relevant information. the following results seeks to accomplish the objectives of calculating the prevalence of AAA within the sample as well as, identifying the correlated risk factors of its occurrence.

4.1.1 AAA prevalence

AAA was observed in 7 patients out of the 680 participants, equating to a prevalence of 1.0% (95% confidence interval 0.4% to 2.1%).

4.1.2 AAA risk factors

The findings of the association between different risk factors and the presence of AAA are displayed in Table 4.1.

The findings revealed statistically significant associations between gender and smoking status (both ever smoked and current smoker) with the occurrence of AAA. Furthermore, there was some indication of a potential correlation between a heart attack and AAA, although this result was only of a borderline statistical significance.

No cases of AAA were detected in females, whereas 2.4% of males exhibited AAA. The results also indicated that current smokers had a significantly higher risk of AAA with a prevalence of 5.8% as opposed to only 0.6% among non-smokers. Moreover, nearly all individuals with AAA had a history of smoking or were current smokers. Patients who had previously experienced a heart attack were found to be at an increased risk of developing AAA. The prevalence of AAA was only 0.7% among patients with no history of heart attack, compared to 3.5% among those who had undergone a heart attack. Figure 4.1 shows a suprarenal AAA in a diabetic patient. Figure 4.2 depicts the prevalence of existing comorbidities within the entire study sample. Figure 4.3 represents the association of AAA with risk factors.

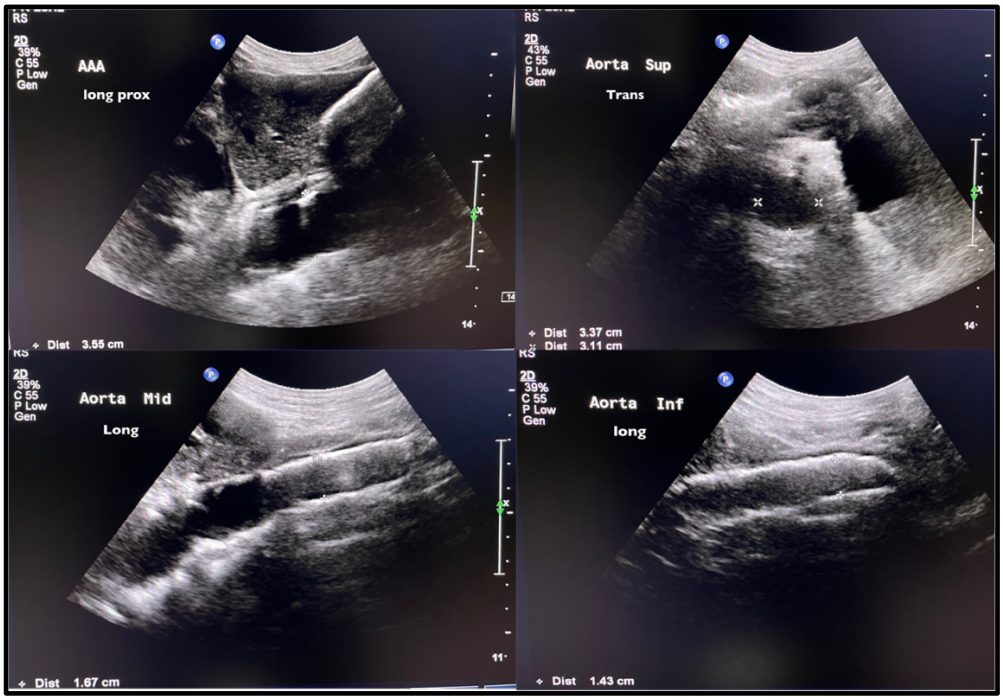


Figure 4. 1 *Ultrasound views of the abdominal aorta in a diabetic patient demonstrating suprarenal AAA (top) and calcified infrarenal aorta (bottom).*

Table 4. 1: *Associations between risk factors and AAA*

Risk factor	Category	No AAA n (%)	AAA n (%)	P-value
Age [(*)]	-	63.3 ± 8.5	66.9 ± 7.9	0.27
Gender	Male	281 (97.6%)	7 (2.4%)	**0.002**
	Female	392 (100.0%)	0 (0.0%)	
Ever smoked	No	540 (99.8%)	1 (0.2%)	**<0.001**
	Yes	133 (95.7%)	6 (4.3%)	
Current smoker	No	624 (99.4%)	4 (0.6%)	**0.01**
	Yes	49 (94.2%)	3 (5.8%)	
Hypertension	No	276 (99.3%)	2 (0.7%)	0.71
	Yes	397 (98.8%)	5 (1.2%)	
Diabetes	No	332 (98.5%)	5 (1.5%)	0.28
	Yes	341 (99.4%)	2 (0.6%)	
High cholesterol	No	236 (100.0%)	0 (0.0%)	0.10
	Yes	437 (98.4%)	7 (1.6%)	

Cardiac arrythmias	No	606 (98.9%)	7 (1.1%)	1.00
	Yes	67 (100.0%)	0 (0.0%)	
Heart attack	No	590 (99.3%)	4 (0.7%)	0.05
	Yes	83 (96.5%)	3 (3.5%)	
Stroke	No	656 (99.1%)	6 (0.9%)	0.17
	Yes	17 (94.4%)	1 (5.6%)	
TIA	No	653 (99.1%)	6 (0.9%)	0.20
	Yes	20 (95.2%)	1 (4.8%)	
Peripheral arterial	No	665 (99.0%)	7 (1.0%)	1.00
disease	Yes	8 (100.0%)	0 (0.0%)	

(*) Mean ± standard deviation reported

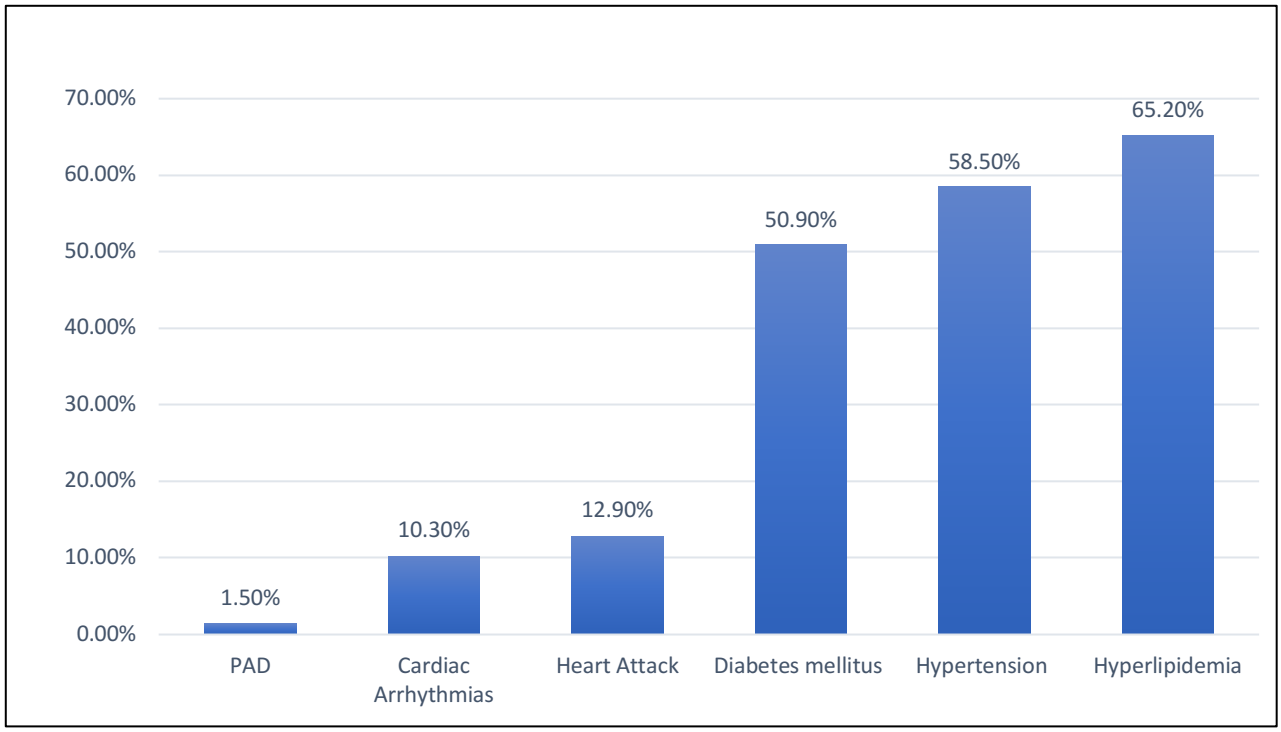


Figure 4. 2 *The percentage of comorbidities in 680 participants. PAD refers to Peripheral Arterial Disease.*

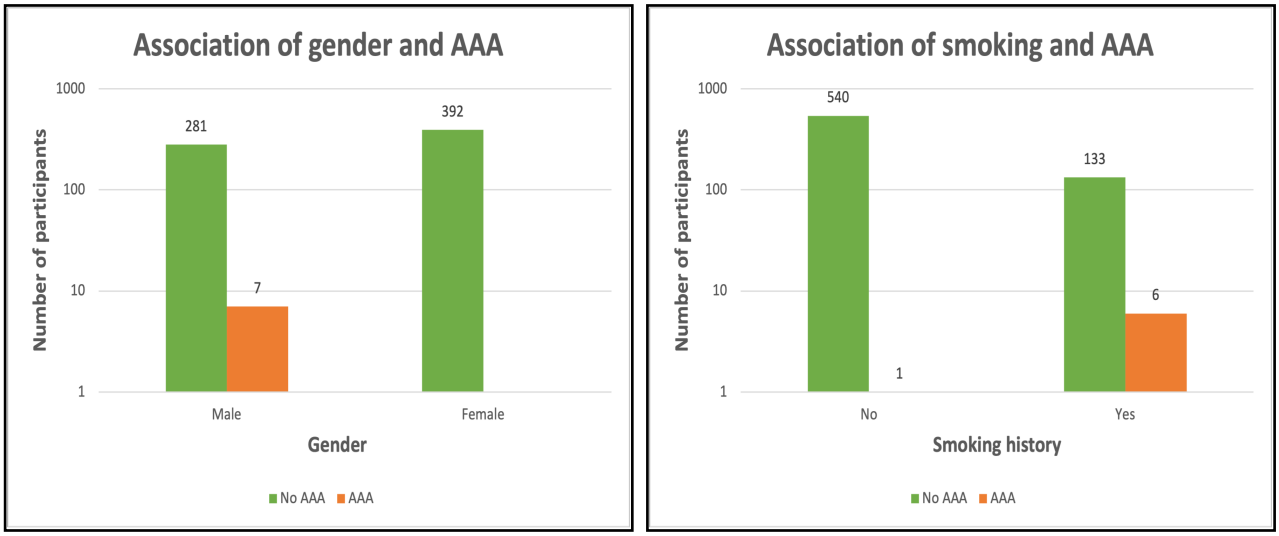


Figure 4. 3 *Bar chart graphs of association of male gender and smoking with AAA.*

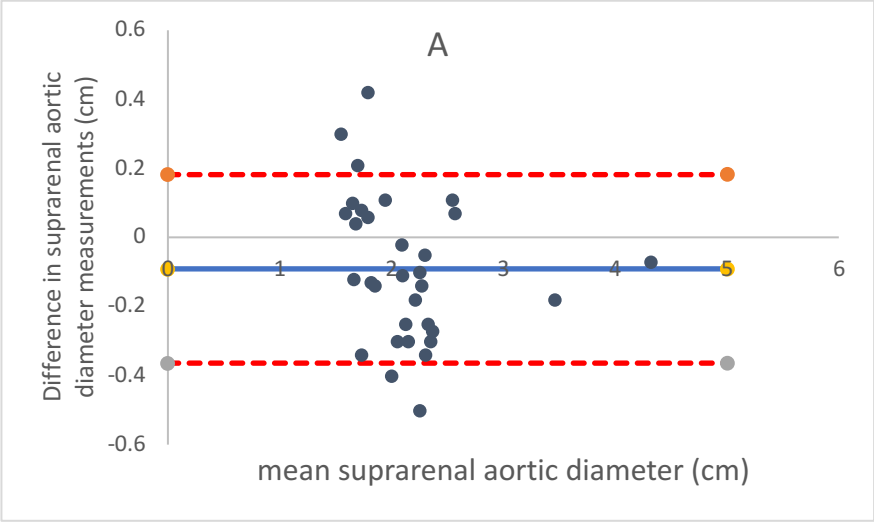
4.1.3 Intra-observer and interobserver agreement

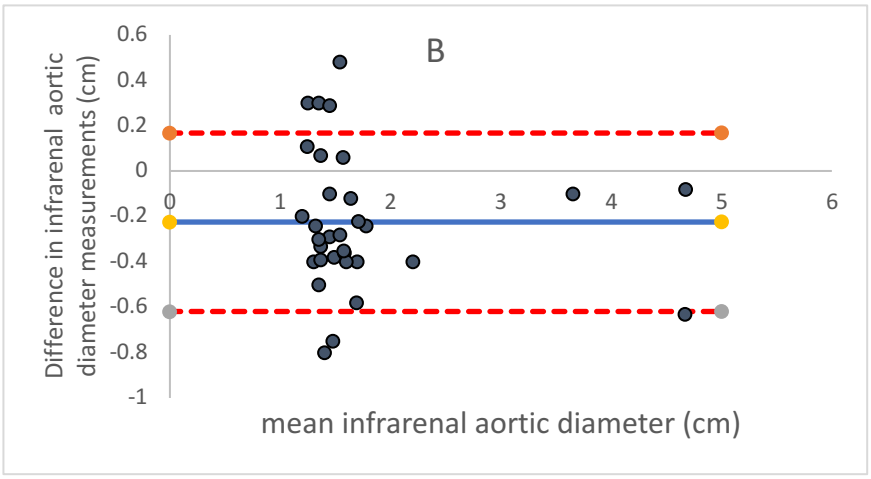
Measurements were obtained from a subset of 32 participants, including those diagnosed with AAA. The interclass correlation coefficients (ICCs) were calculated to assess the reproducibility of both intra- and inter-observer diameter measurements of the suprarenal, infrarenal, and distal aorta. The ICC values for the intra-observer agreement were 0.96, 0.92, and 0.95 for the suprarenal, infrarenal, and distal aorta, respectively, indicating excellent agreement. An ICC value greater than 0.9 is considered to have excellent reliability. The ICC values for the inter-observer agreement were 0.88, 0.85, and 0.89 for the suprarenal, infrarenal, and distal aorta, respectively, indicating good agreement. An ICC value between 0.75 and 0.9 is considered to have good reliability (Koo & Li, 2016). In Table 4.2, the interclass correlation coefficients for intra and interobserver reliability are presented. To examine the agreement between aortic diameter measurements made by intra- and inter-observers, Bland-Altman plots were generated, thereby providing a useful visual representation of the agreement. The resulting plots indicated good agreement and are presented in Figures 4.4 and 4.5, respectively.

Table 4. 2: *The interclass correlation coefficients for the intra and interobserver reproducibility*

Reliability metric	ICC	95% Confidence Interval
Intra-observer reproducibility (Suprarenal Aorta)	0.96	0.92- 0.98
Intra-observer reproducibility (Infrarenal Aorta)	0.92	0.84 – 0.96

Intra-observer reproducibility (Distal Aorta)	0.95	0.89 – 0.97
Interobserver reproducibility (Suprarenal Aorta)	0.88	- 0.98 –0.97
Interobserver reproducibility (Infrarenal Aorta)	0.85	- 0.14 – 0.96
Interobserver reproducibility (Distal Aorta)	0.89	0.68 – 0.9





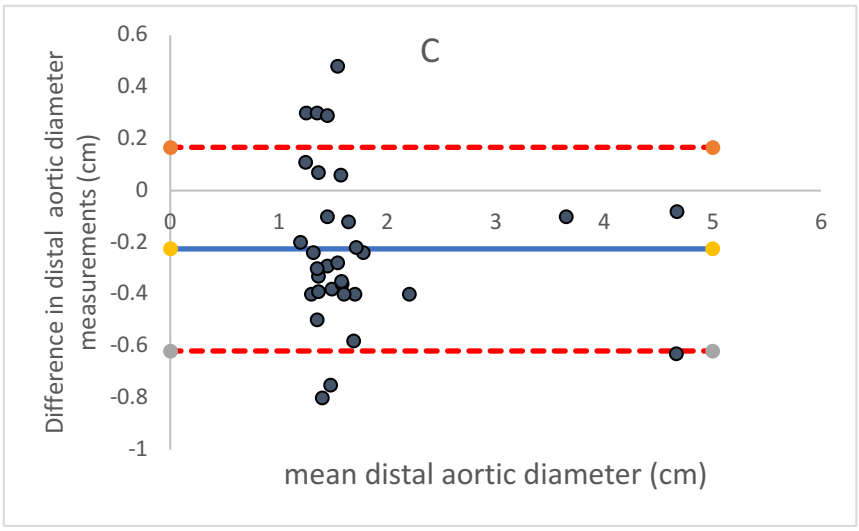
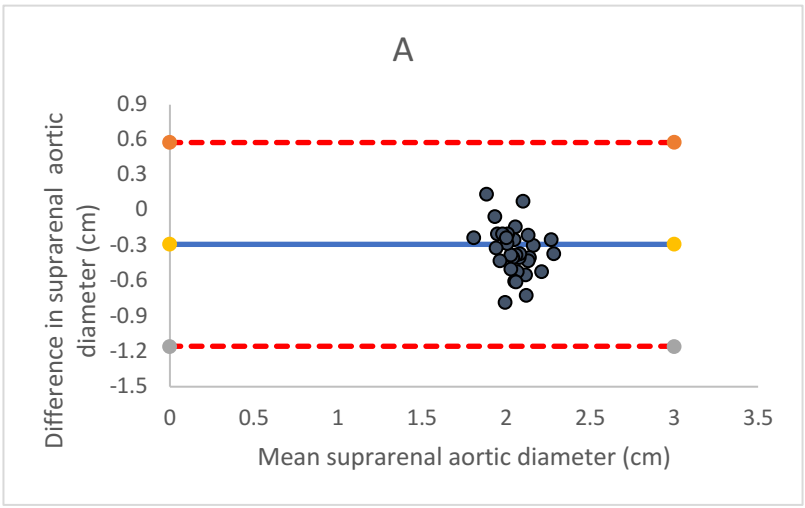


Figure 4. ***4*** *Bland-Altman plots for suprarenal (A), infrarenal (B), and distal(C)aortic diameter, showing the agreement between intra-observer measurements, with the horizontal line representing the mean difference between the two measurements and the dotted lines indicating the limits of agreement.*



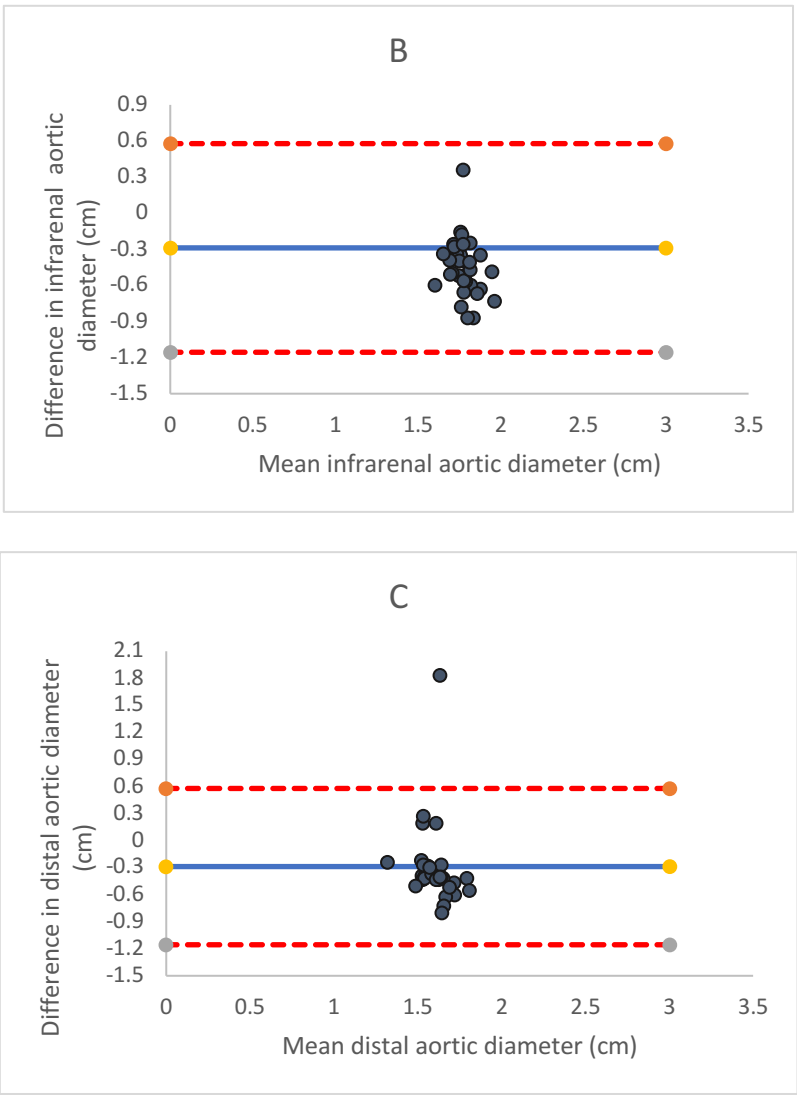


Figure 4. 5 *Bland-Altman plots Bland-Altman plots for suprarenal (A), infrarenal (B), and distal(C)aortic diameter, showing the agreement between inter-observer measurements, with the horizontal line representing the mean difference between the two measurements and the dotted lines indicating the limits of agreement.*

4.2 Shear wave elastography study

This study investigated elastic properties of aneurysmal and non-aneurysmal aortic walls using SWE ultrasound in 100 patients, including 50 AAA cases and 50 controls. collected from a total of 100 patients, 50 AAA cases and 50 controls.

4.2.1 Associations between risk factors and presence of AAA

The initial analyses involved determining the relationship between each risk factor and the case/control status, with the results being shown in Table 4.3.

Table 4. 3 *Associations between risk factors and presence of AAA*

Factor	Controls (N=50)	AAA cases (N=50)	Odds Ratio (95% CI)	P-value
Age (*)	72.1 ± 9.2	72.1 ± 9.0	1.00 (0.65, 1.55)	0.98
Male sex	51 (100%)	51 (100%)	-	-
Weight (kg) (*)	74.8 ± 7.5	78.1 ± 10.4	1.50 (0.96, 2.35)	0.07
Height (cm) (*)	171.8 ± 3.7	172.9 ± 4.8	1.91 (0.74, 4.92)	0.18
Diabetes	3 (6%)	14 (27%)	6.05 (1.62, 22.6)	**0.007**
CAD	4 (8%)	18 (35%)	6.41 (1.99, 20.7)	**0.002**
Hypertension	25 (49%)	35 (69%)	2.28 (1.02, 5.10)	0.05
High cholesterol	22 (43%)	34 (67%)	2.64 (1.18, 5.89)	**0.02**
Smoker	18 (35%)	26 (51%)	1.91 (0.86, 4.22)	0.11

Summary statistics are mean ± standard deviation, or number (percentage), CAD refers to coronary artery disease.

The findings suggested that diabetes, coronary artery disease (CAD), and high cholesterol were significantly associated with AAA. The results demonstrated some evidence that weight and hypertension were also associated with this outcome, although the results for these factors were only of borderline statistical significance (Figure 4.6).

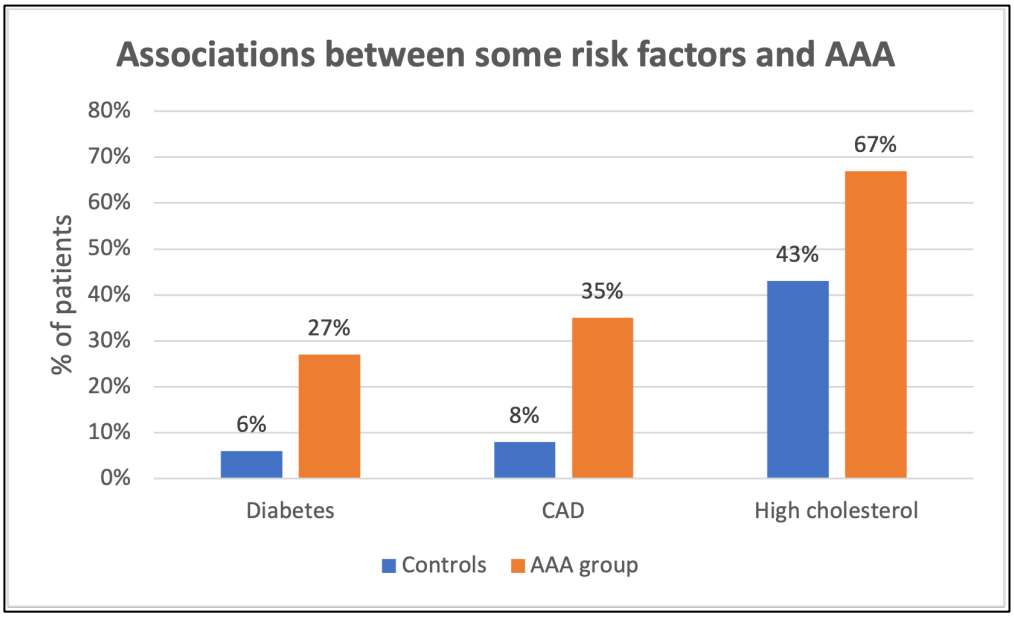


Figure 4. 6 *Bar chart graph showing the associations of AAA with some risk factors.*

The study revealed that the presence of diabetes and CAD was linked with a substantial increase in the risk of AAA. Patients with these factors exhibited 6 times higher odds AAA when compared to those without these factors. Furthermore, patients with high cholesterol had 2.6 times higher odds of AAA compared to those without high cholesterol.

The subsequent analyses focused on investigating the joint association between the risk and AAA in a multivariable analysis. This aimed to distinguish between factors that were independently associated with AAA and those that exhibited significance due to their associations with other factors.

Only factors displaying some association with AAA in the initial analyses were included in this analysis. To drive a final regression model, a backwards selection procedure was used, which kept only factors exhibiting significant association with the outcome. A summary of the final model is provided in Table 4.4.

Table 4. 4 *Multivariable associations with presence of AAA*

Factor	Odds Ratio (95% CI)	P-value
Diabetes	3.64 (0.85, 15.6)	0.08
CAD	3.58 (1.00, 12.7)	0.05
High cholesterol	2.21 (0.93, 5.89)	0.07

The results indicated borderline statistical significance for diabetes, CAD, and high cholesterol as independent factors associated with AAA. However, the results were only of marginal statistical significance for all factors. Again, the presence of each factor was associated with a higher chance of AAA. The effect of each factor after adjusting for the other factors was lower than in the initial (univariable) analyses. The odds of AAA for patients with either diabetes or CAD were over three times higher than for patients without these factors.

A visual representation of the association is depicted in Figure 4.7.

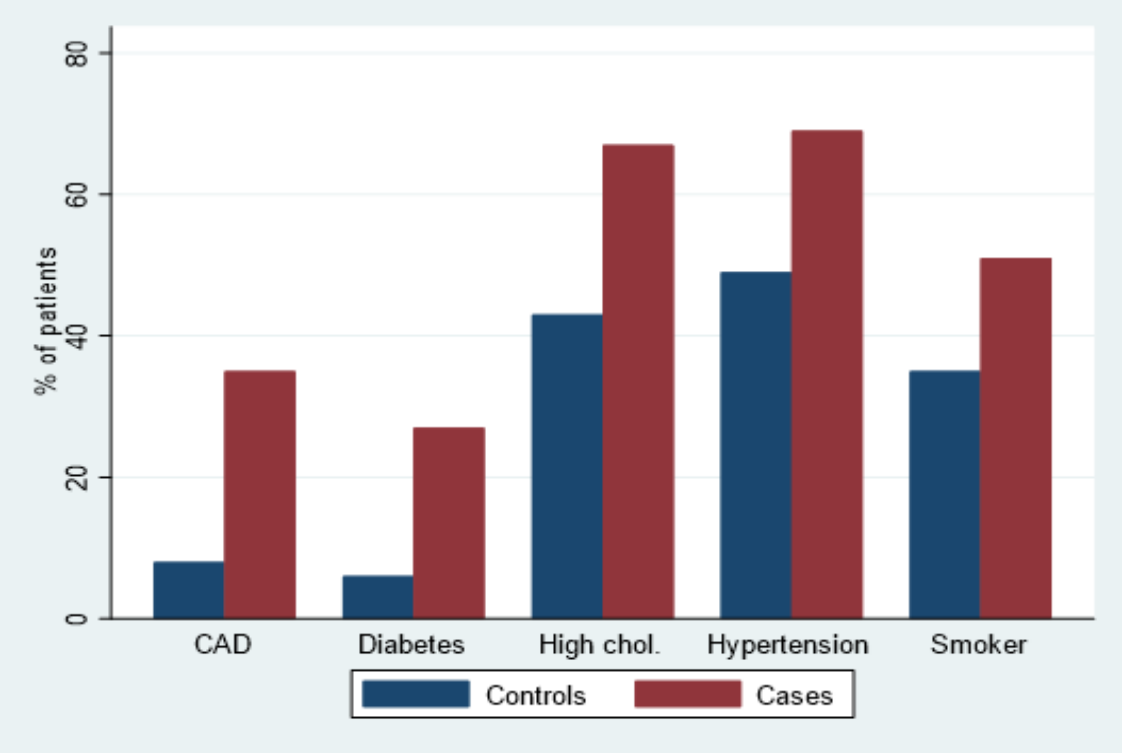


Figure 4. *7 Associations between some risk factors and AAA, CAD refers to coronary artery disease.*

4.2.2 Arterial stiffness

The primary objective of the study's final analysis was to assess the degree to which the artery wall stiffness of the two groups was comparable. Table 4.5 contains a summary of the findings, which includes the mean and standard deviation stiffness values for each group, in addition to the difference in stiffness values across the groups (and corresponding confidence interval). The last column provides a p-value, which indicates the degree to which the statistical difference between the groups is significant.

Table 4. 5 *Arterial Stiffness in Cases and Controls*

Group	n	Arterial Stiffness (Kpa) Mean ± SD	Difference Mean (95% CI)	P-value
Controls AAA cases	50 50	70 ± 12 29 ± 8	0 -41 (-45, -37)	**<0.001**

The study finding revealed a highly significant statistical difference in arterial wall stiffness between the cases and controls, with condsiderably lower valuses observed in the AAA cases exhibiting a mean of 29 Kpa, as opposed to a mean of 70 Kpa in controls. This suggests that AAA walls are more elastic.

A visual representation of the results is depicted in Figure 4.8.

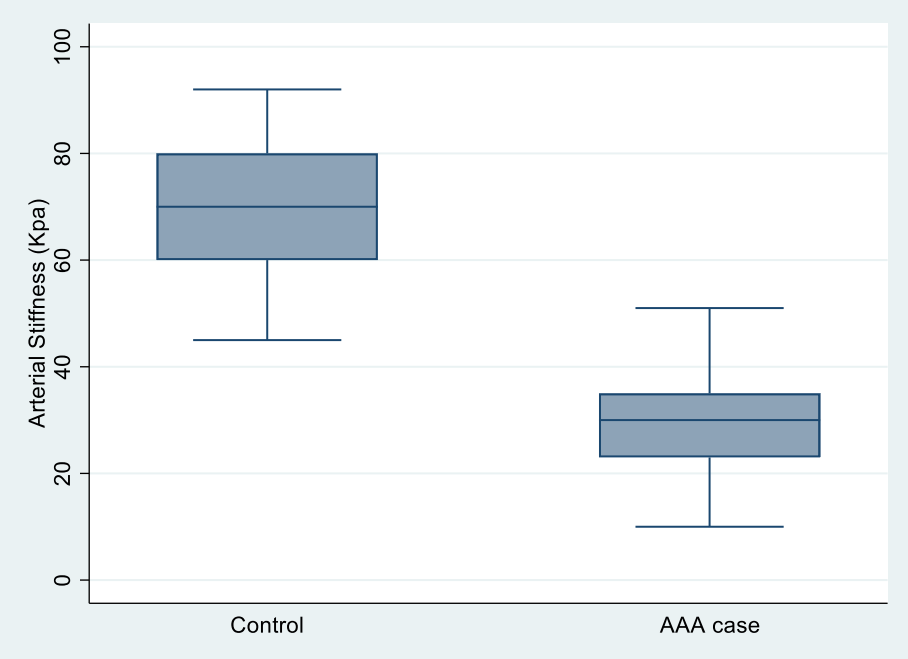


Figure 4. 8 *Boxplot of Arterial Stiffness in the two study groups.*

4.3 Butterfly iQ study

The study assessed aortic diameter measurements obtained by Butterfly iQ probe and conventional ultrasound machines in patients with AAA. It quantified the level of agreement between the two methods.

4.3.1 Patient characteristics

Thirteen patients were included in this study and a summary of their characteristics is presented in Table 4.6.

The study population exhibited a mean age of 73 ± 10.4 years, with a predominant male representation (85%). Approximately one–quarter (23%) of the patients were current smokers, while nearly one-third (31%) had never smoked. A proportion of the patients had diabetes, with slightly over one-quarter affected, while over two-thirds had hypertension (Figure 4.9).

Table 4. 6 Patient characteristics

Risk factor	n	Category	Summary
Age	13	-	73.1 ± 10.4
Gender	13	Male	11 (85%)
		Female	2 (15%)

BMI	13	-	26.1 ± 4.2
Smoking status	13	Never smoked	4 (31%)
		Ex-smoker	6 (46%)
		Current smoker	3 (23%)
Smoking duration (yrs) (*)	9	-	40 ± 10
Smoking packets / day (*)	5		2.3 ± 1.3
Diabetes	13	No	10 (77%)
		Yes	3 (23%)
Hypertension	13	No	4 (31%)
		Yes	9 (69%)
High cholesterol	13	No	6 (46%)
		Yes	7 (54%)

Summary statistics are mean ± standard deviation, or number (percentage)

(*) Figures for ex and current smokers only

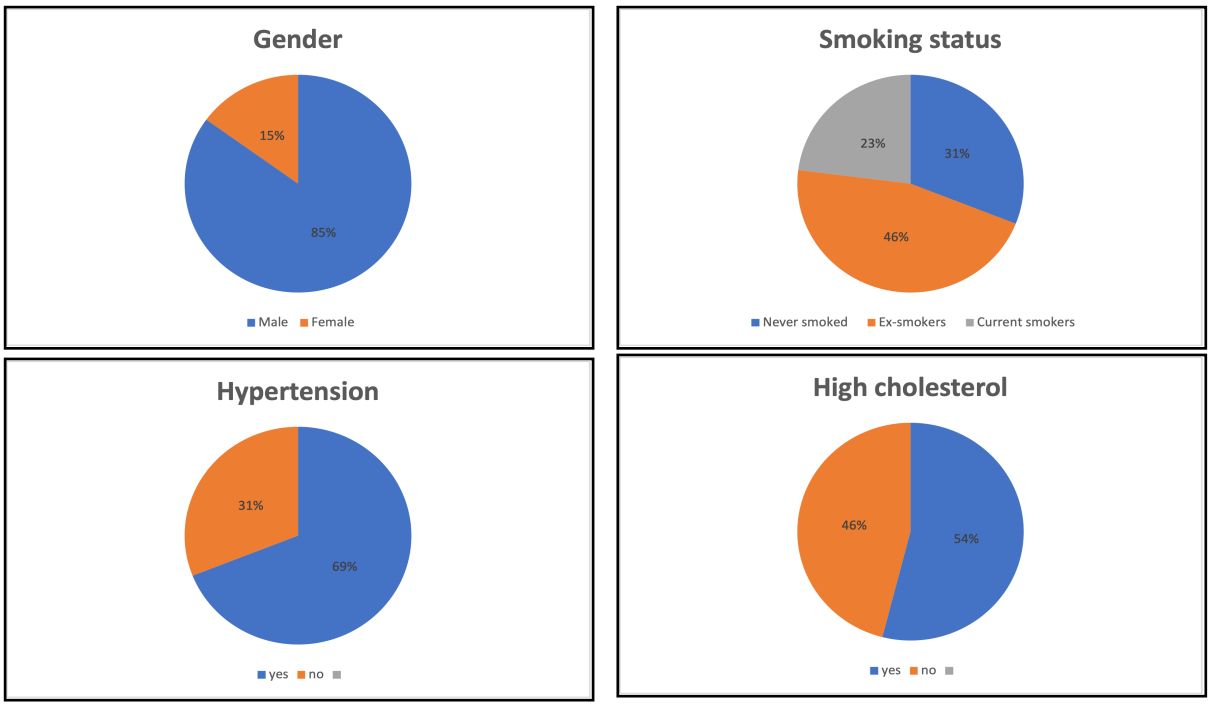


Figure 4. 9 Pie chart graphs of the patient characteristics.

4.3.2 Inter-system agreement

This analysis aimed to assess the level of agreement between the conventional ultrasound machine and the Butterfly iQ probe. The Bland-Altman method was initially employed to evaluate the size of agreement between the two methods. The calculations were performed on the first measurement obtained by each observer and then repeated for the mean of three measurements. The summary of the analysis results is presented in Table 4.7, which includes the mean difference between the Butterfly and conventional ultrasound machine (calculated as Butterfly minus conventional), the standard deviation of the differences, and the 95% limits of agreement according to the Bland-Altman method.

***Table 4.** 7 Agreement between methods (Bland-Altman method)*

Observer	Outcome	Data	Difference (Butterfly – Conventional)		95% Bland-Altman limits of agreement
			Mean	SD	
1	Proximal	Measurement 1	-0.07	0.25	-0.56, 0.43
		Mean	-0.06	0.35	-0.75, 0.63
	Distal	Measurement 1	0.02	0.36	-0.68, 0.72
		Mean	-0.05	0.36	-0.75, 0.65
2	Proximal	Measurement 1	0.01	0.32	-0.61, 0.63
		Mean	-0.1	0.27	-0.63, 0.42
	Distal	Measurement 1	-0.11	0.33	-0.76, 0.53
		Mean	-0.14	0.25	-0.62, 0.34

Analysis of the results revealed mean differences close to zero for both proximal and distal measurements. This implies that, on average, there was no systematic difference in measurements obtained by either machine, indicating that neither probe was consistently producing higher of lower measurements than the other.

The primary outcome of interest is the width of the Bland-Altman limits of agreement, which indicates the range within which most differences between the measurements obtained by the two machines fall. The width of the Bland Altman limits was, typically, similar for the proximal and distal measurements and for the two observers. The width of the intervals was slightly wider than those observed for the inter-observer and intra-observer agreement (results presented in the following sections).

The results can be displayed graphically in Bland-Altman plots, which plot the differences in measurements between machines against the average of measurement by two machines. Figures 4.10 and 4.11 show the results for the proximal measurements from observer 1 (Fig 4.10 shows measurement 1, Fig 4.11 the mean of the measurements). Figures 4.12 and 4.13 show the distal results, again just for observer 1. In each graph, the three lines marked are the upper and lower limits of agreement (in red), and the mean difference between the two probes (in blue).

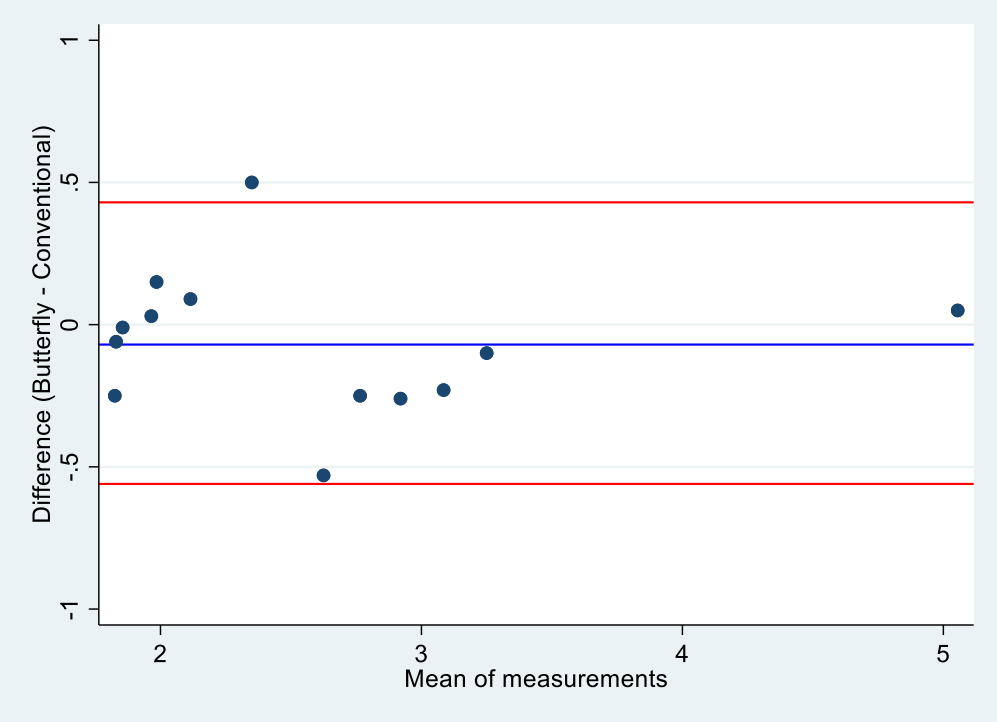


Figure 4. 10 *Bland-Altman limits of agreement for Observer 1*

(Proximal, measurement 1)

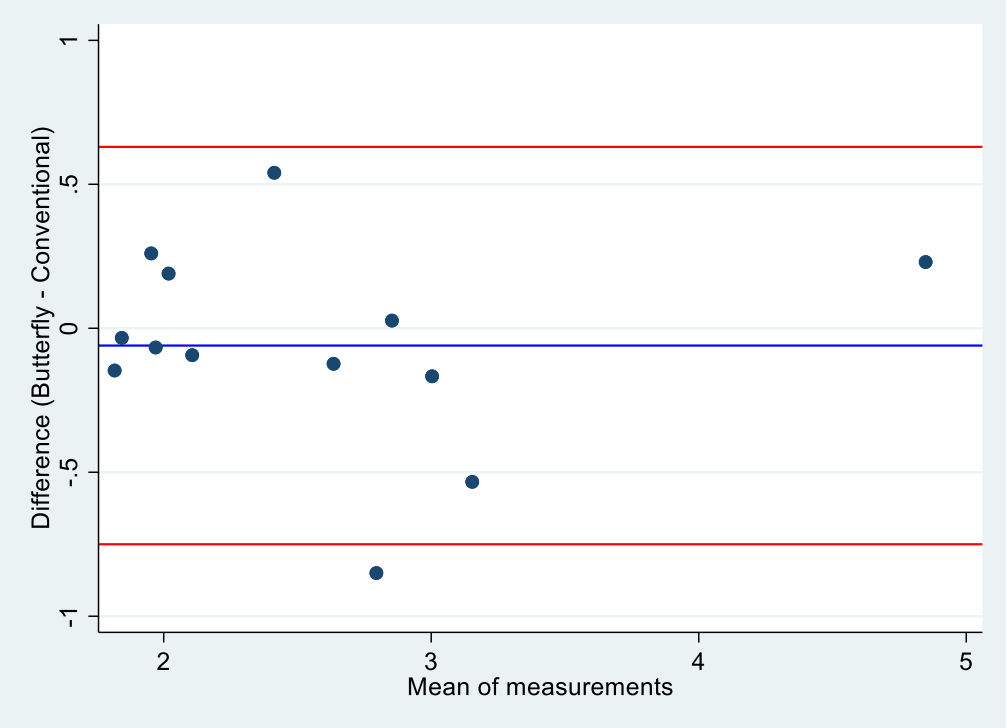


Figure 4. 11 *Bland-Altman limits of agreement for Observer 1*

(Proximal, mean of measurement)

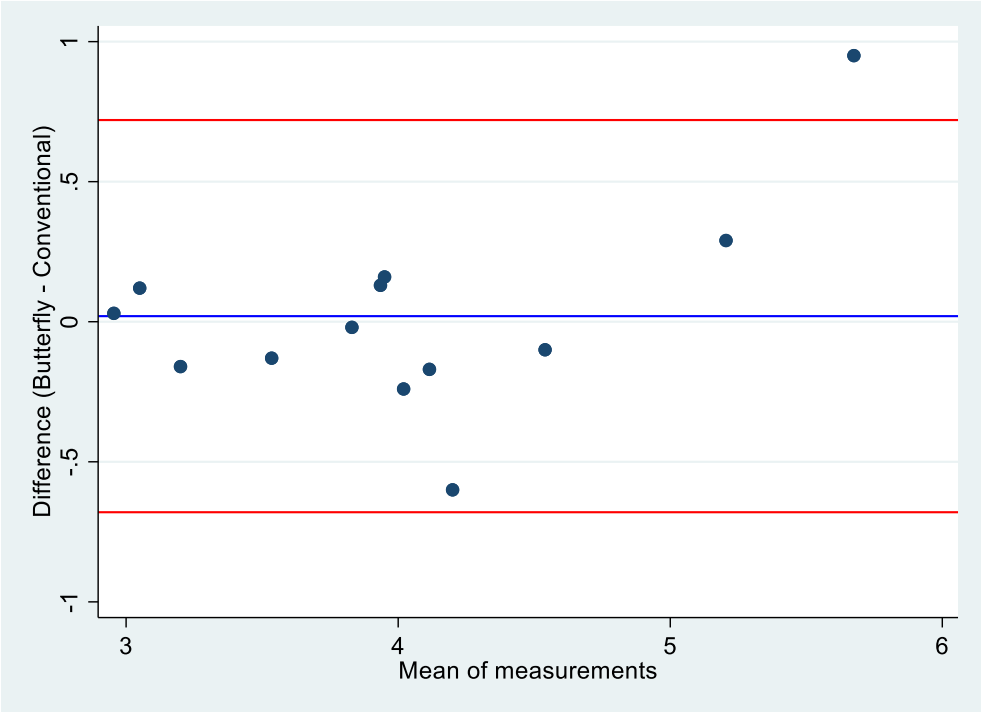


Figure 4. 12 *Bland-Altman limits of agreement for Observer 1*

(Distal, measurement 1)

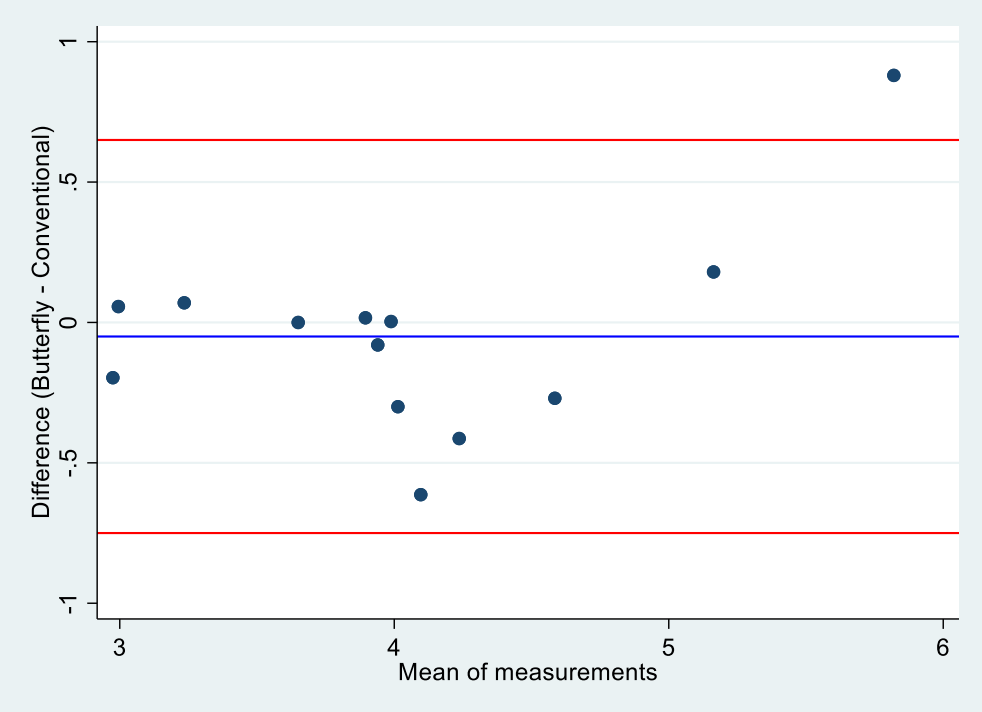


Figure 4. 13 *Bland-Altman limits of agreement for Observer 1*

(Distal, mean of measurements)

The level of agreement between the two methods was also evaluated using the intra-class correlation (ICC) method. The analysis results are presented in Table 4.8, which includes the calculated ICC values along with their corresponding confidence intervals.

Table 4. 8 *Agreement between methods (ICC method)*

Observer	Outcome	Data	ICC (95% CI)
1	Proximal	Measurement 1	0.96 (0.88, 0.99)
		Mean	0.92 (0.76, 0.97)
	Distal	Measurement 1	0.91 (0.74, 0.97)
		Mean	0.91 (0.75, 0.97)
2	Proximal	Measurement 1	0.93 (0.79, 0.98)
		Mean	0.94 (0.81, 0.98)
	Distal	Measurement 1	0.91 (0.74, 0.97)
		Mean	0.94 (0.82, 0.98)

The findings indicated a high level of agreement between the two observers for both the Conventional and Butterfly iQ machines, with all ICC values exceeding 0.9 for both first measurement and the mean of three measurements. The level of agreement was relatively consistent for both proximal and distal measurements. Despite that, the level of agreement

between the two probes was slightly lower compared to the intra-observer and inter-observer agreement, as presented in the following sections.

The final analysis aimed to quantify the proportion of the pairs of measurements where the agreement between the two machines fell within pre-defined limits (ranging from≤1mm up to ≤4mm). the outcomes are presented in Table 4.9.

Table 4. 9 *Percentage of pairs of measurements with differences between Conventional and Butterfly probes within pre-defined limits*

location	Data	% Pairs within limits			
		≤1mm	≤2mm	≤3mm	≤4mm
Proximal	Measurement 1	38%	46%	73%	85%
	Mean	27%	62%	77%	81%
Distal	Measurement 1	12%	58%	77%	85%
	Mean	35%	65%	77%	85%

4.3.3 Intra-observer agreement

The size of the intra-observer agreement was initially evaluated using the Bland-Altman method. The analysis outcomes are presented in Table 4.10, reporting the mean difference between the two sets of measurements (calculated as measurement 2 minus measurement 1), the standard deviation of the differences, and the 95% limits of agreement.

The outcomes indicated mean differences close to zero for both machines, suggesting that the second measurement is not typically higher or lower than the first. The primary finding of interest is the width of the Bland-Altman limits of agreement, which represents the range within which most differences between measurements occur. The actual width of the limits varies depending on the probe, outcome, and observer. The width of the B-A limits was, typically, similar for the conventional and butterfly methods, suggesting a similar level of intra-observer agreement for both. The results were also similar for proximal and distal measurements.

Table 4. 10 *Intra-observer agreement (Bland-Altman method)*

Probe	Outcome	Observer	Difference (measure 2 – measure 1)		95% Bland-Altman limits of agreement
			Mean	SD	
Conventional	Proximal	1	-0.04	0.25	-0.53, 0.46
		2	-0.02	0.16	-0.33, 0.29
	Distal	1	0.09	0.19	-0.28, 0.45
		2	-0.06	0.28	-0.60, 0.49

Butterfly	Proximal	1	-0.03	0.19	-0.40, 0.33
		2	-0.06	0.37	-0.79, 0.66
	Distal	1	0.01	0.18	-0.34, 0.36
		2	-0.12	0.31	-0.72, 0.48

The results can be visually represented through Bland-Altman plots. Figures 4.14 and 4.15 illustrate the proximal measurements obtained by observer 1 using different probes. The three lines demarcated on the plot represent the upper and lower limits of agreement (highlighted in red) and the mean difference between the two pairs of measurements (shown in blue).

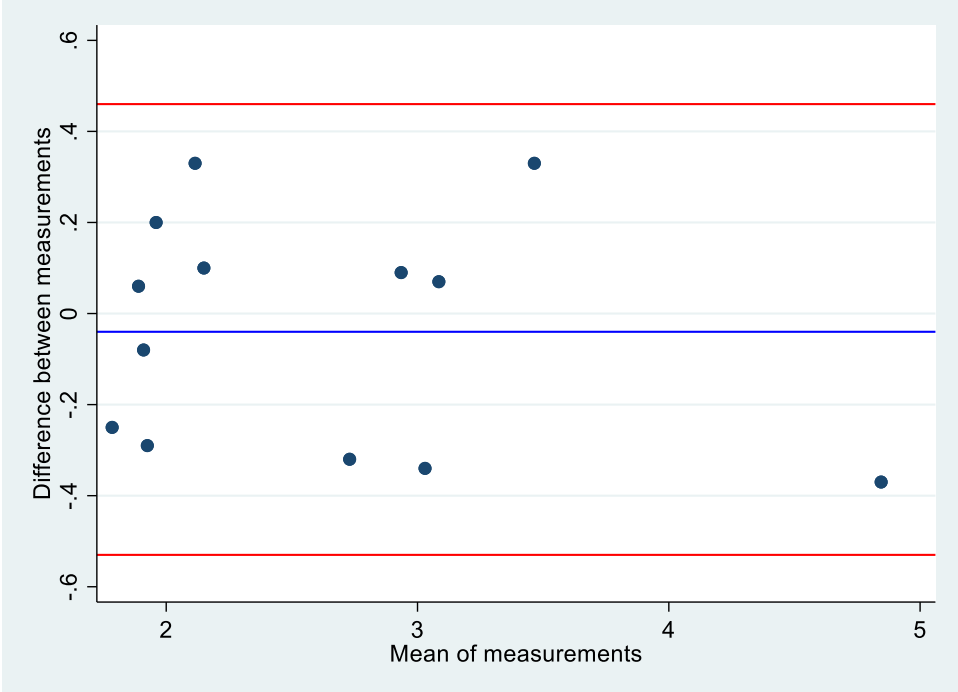


Figure 4. **14** *Bland-Altman limits of agreement for Conventional Probe*

(Observer 1, proximal measurement)

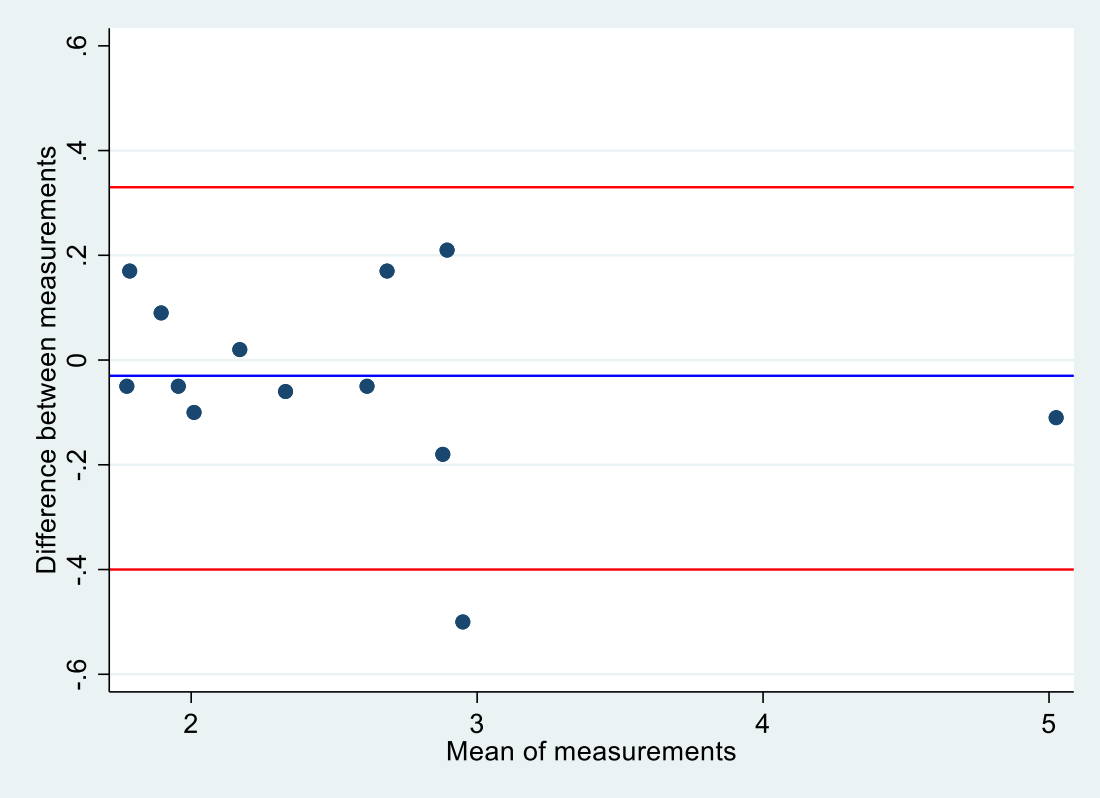


Figure 4. 15 *Bland-Altman limits of agreement for Butterfly Probe*

(Observer 1, proximal measurement)

The level of intra-observer agreement was also evaluated using the intra-class correlation (ICC) method. The finding relating to the intra-observer agreement are presented in Table 4.11, which includes the calculated values and their corresponding confidence intervals.

Table 4. 11 *Intra-observer agreement (ICC method)*

Probe	Outcome	Observer	ICC (95% CI)
Conventional	Proximal	1	0.94 (0.85, 0.98)
		2	0.86 (0.69, 0.95)
	Distal	1	0.97 (0.92, 0.99)
		2	0.91 (0.79, 0.97)
Butterfly	Proximal	1	0.98 (0.94, 0.99)
		2	0.91 (0.79, 0.97)
	Distal	1	0.98 (0.95, 0.99)
		2	0.94 (0.87, 0.98)

The outcomes indicated a high level of agreement between the repeated measurements obtained using both conventional and butterfly machines for both the proximal and distal measurements. The majority of ICC values were above 0.9. There were similar ICC values for the conventional and butterfly probes, suggesting similar levels of intra-observer agreement for both methods.

4.3.4 Inter-observer agreement

Similar analysis methods were used to assess the size of the inter-observer agreement for the two probes. The results are summarized in Table 4.12.

Table 4. 12 *Inter-observer agreement (Bland-Altman method)*

Probe	Outcome	Data	Difference (observer 2 – observer 1)		95% Bland-Altman limits of agreement
			Mean	SD	
Conventional	Proximal	Measurement 1	-0.01	0.29	-0.57, 0.55
		Mean	0.06	0.29	-0.50, 0.63
	Distal	Measurement 1	-0.02	0.20	-0.24, 0.53
		Mean	-0.08	0.22	-0.51, 0.34
Butterfly	Proximal	Measurement 1	0.07	0.21	-0.35, 0.49
		Mean	0.02	0.24	-0.45, 0.49
	Distal	Measurement 1	-0.16	0.28	-0.71, 0.40
		Mean	-0.17	0.30	-0.76, 0.42

For most analyses, there was relatively little difference on average between the observers. The exception was for the distal measurements for the Butterfly probe, where observer 2 had lower measurements than observer 1, by a mean of around 0.16 units. The width of the Bland-Altman limits was similar for proximal and distal measurements, and similar for the two probes. Graph illustrations of the inter-observer agreement, for measurement 1, are shown in Figures 4.16 to 4.19.

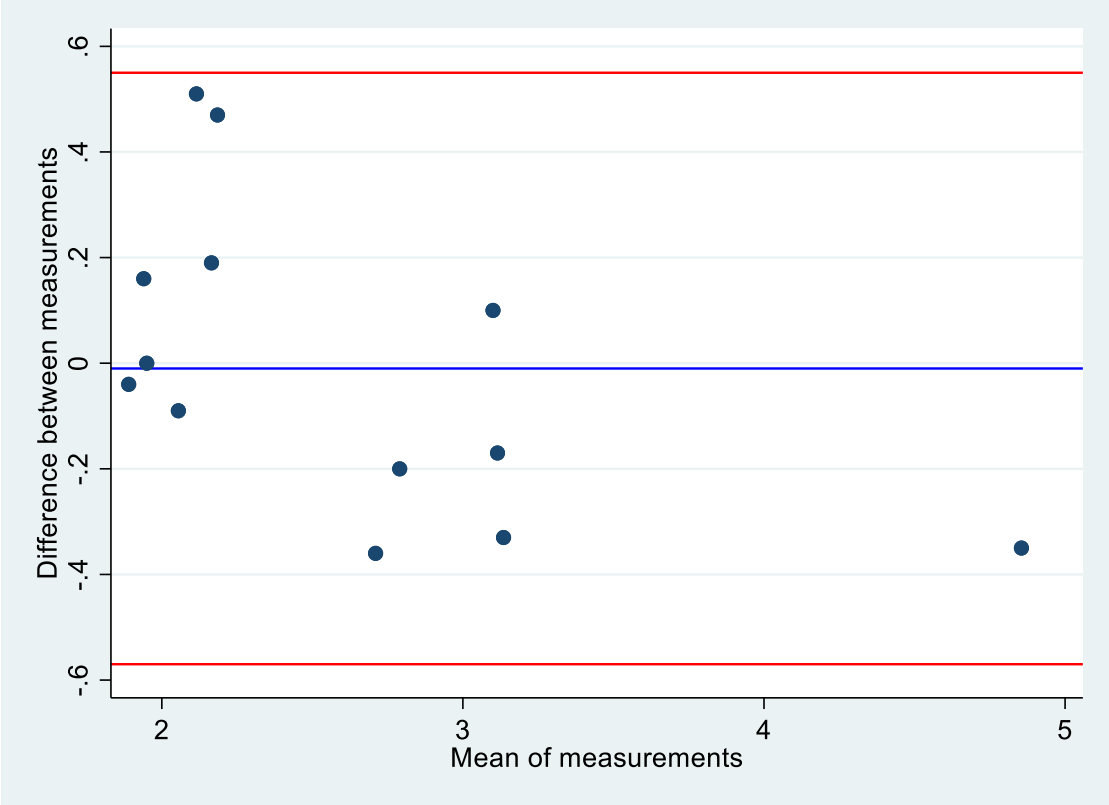


Figure 4. 16 *Bland Altman limits of agreement for Conventional probe, proximal measurement (measurement 1*)

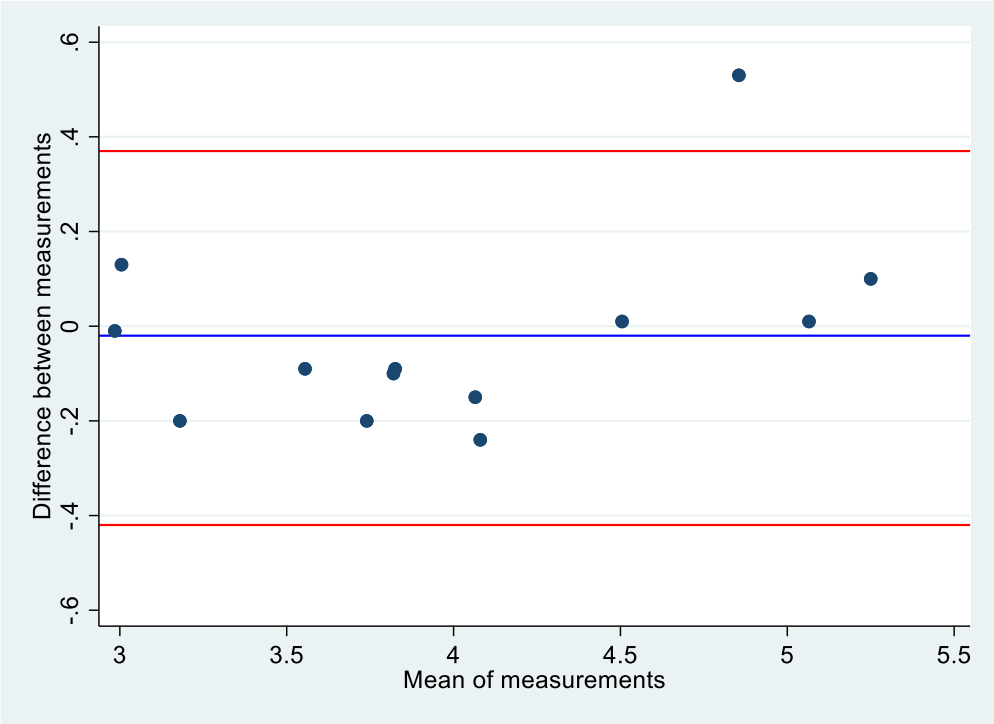


Figure 4. 17 *Bland Altman limits of agreement for Conventional probe, distal measurement (measurement 1)*

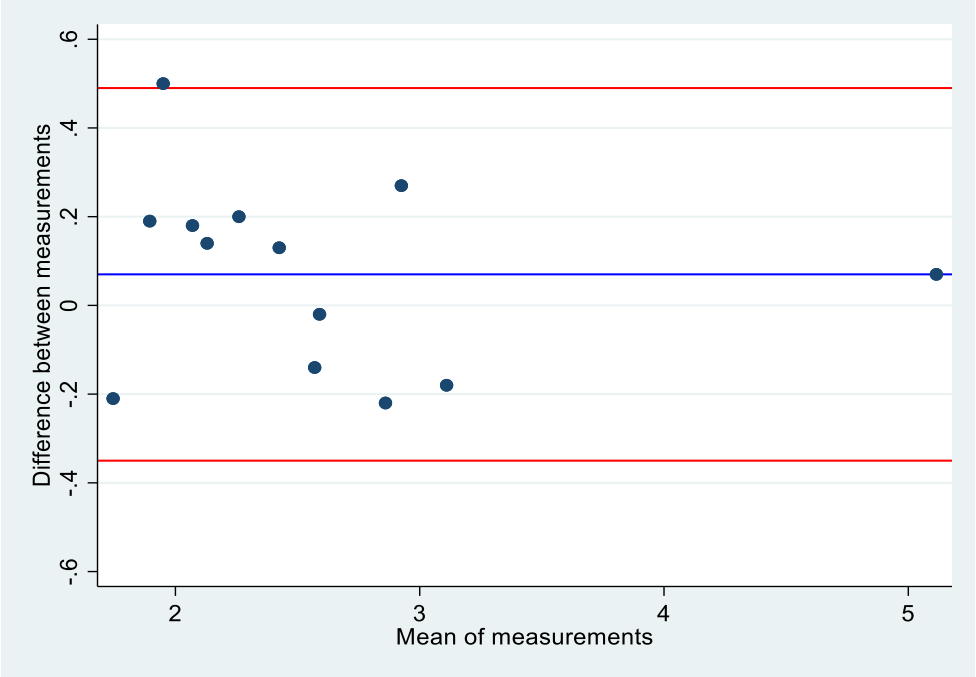


Figure 4. 18 *Bland Altman limits of agreement for Butterfly probe, proximal measurement (measurement 1)*

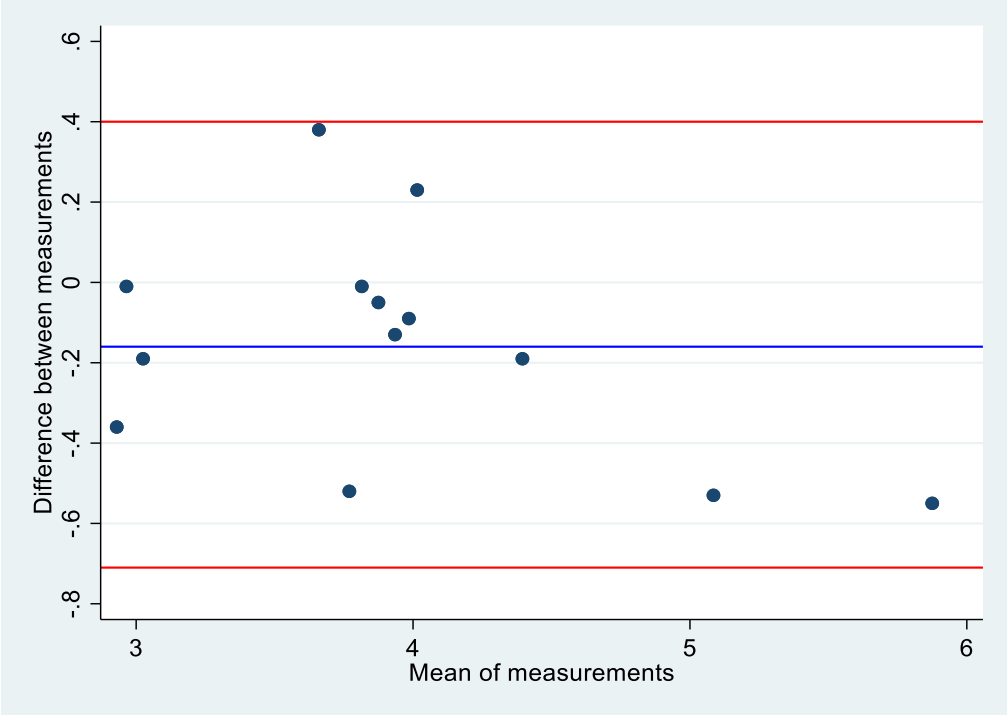


Figure 4. 19 *Bland Altman limits of agreement for Butterfly probe, distal measurement (measurement 1)*

The inter-observer agreement was evaluated using the intra-class correlation (ICC) method as well, and the findings are presented in Table 4.13.

Table 4. 13 *Inter-observer agreement (ICC method)*

Probe	Outcome	Data	ICC (95% CI)
Conventional	Proximal	Measurement 1	0.95 (0.84, 0.98)
		Mean	0.94 (0.82, 0.99)

	Distal	Measurement 1	0.97 (0.90, 0.99)
		Mean	0.96 (0.87, 0.99)
Butterfly	Proximal	Measurement 1	0.97 (0.91, 0.99)
		Mean	0.96 (0.87, 0.99)
	Distal	Measurement 1	0.93 (0.80, 0.98)
		Mean	0.92 (0.87, 0.99)

The results suggested very good agreement between the two observers for both the Conventional and Butterfly probes. All ICC values, for both measurement 1 and the mean of the three measurements, were over 0.9. There was a relatively similar level of agreement for both probes.

Agreement between the two observers was generally comparable in magnitude to the intra-observer agreement.

A series of box plots were used to visually represent the proximal and distal diameter measurements. The proximal and distal measurements of observer 1 were presented in Figure 4.20 and the measurements of observer 2 were represented in Figure 4.21. Each plot displays the repeated measurements for each of the two probes.

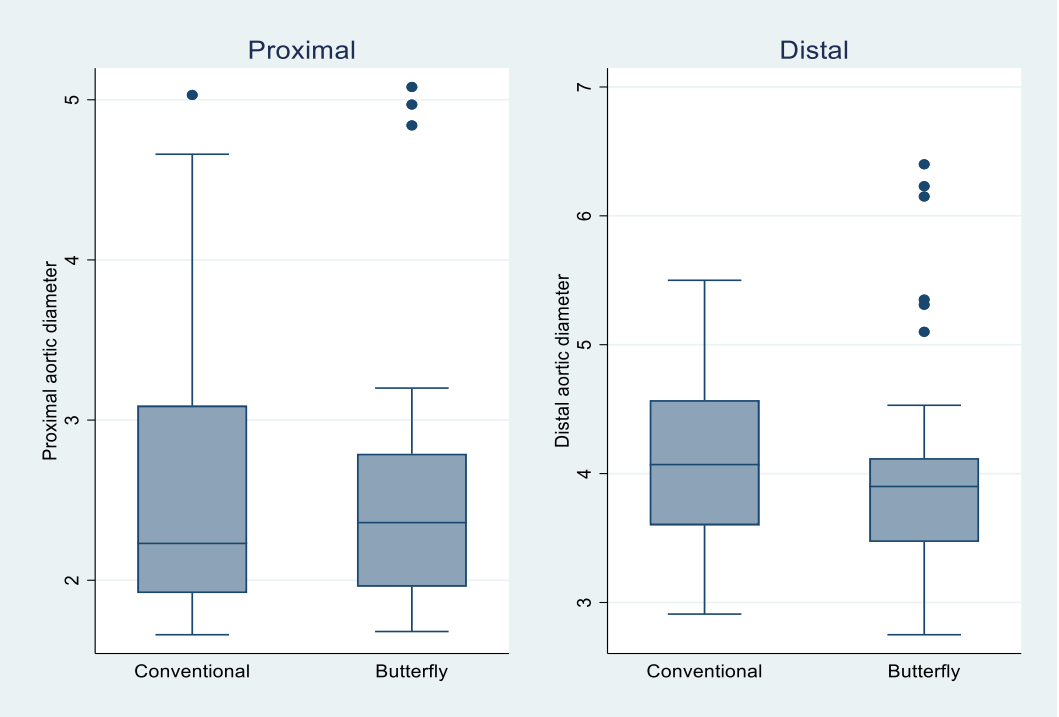


Figure 4. 20 *Observer 1 aortic measurements at proximal (left) and distal (right) Locations using the conventional system and the Butterfly iQ handheld ultrasound device.*

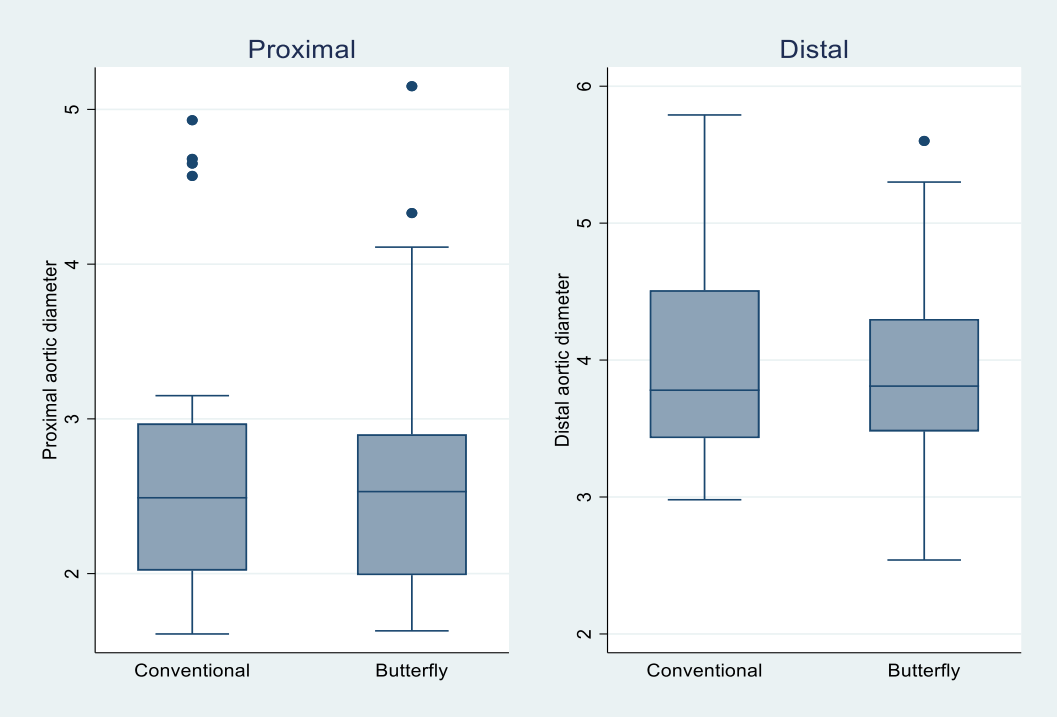


Figure 4. 21 *Observer 2 aortic measurements at proximal (left) and distal (right) Locations using the conventional system and the Butterfly iQ handheld ultrasound device.*

CHAPTER 5: Discussion

This chapter will reflect on research findings and evaluate their significance in relation with existing knowledge in the literature. furthermore, it will discuss the research limitations and offer suggestions for future research directions, to enhance the understanding of AAA under investigation.

5.1 Introduction

AAA presents a significant burden on both patients and health care systems, as it is estimated to affect up to 5% of men over the age of 65 in Western countries with a mortality rate as high as 80% if AAA ruptures before reaching the hospital (Golledge et al., 2006) (Reimerink et al., 2013). Ultrasound is largely considered to be the primary imaging method required for screening, initial diagnosis, and AAA surveillance. AAA screening in elderly men is cost-effective and reduces rupture mortality rates, according to evidence-based studies conducted in Western countries (Altobelli et al., 2018). In Saudi Arabia, there has been little research on AAA screening. Therefore, establishing a national AAA screening program may reduce the mortality rate due to AAA rupture, explore epidemiological risk factors associated with AAA development, and enable comparison with similar studies conducted on other ethnic groups in Western countries. This research is comprised of three parts; the screening study aims to provide significant information on the prevalence of AAA among Saudi Arabia's population, especially residents of Riyadh, to establish screening requirements customized to the Saudi population. SWE ultrasound has the potential to provide valuable diagnostic and monitoring information regarding the elastic properties of the abdominal aortic wall. This study compared the stiffness of the aortic wall between aneurysmal and non-aneurysmal aortas to enhance the practice of AAA identification and deliver better patient outcomes by allowing a more accurate estimate of the risk of disease progression. Ultrasound is the modality of choice for screening.

Portable ultrasound devices such as the Butterfly iQ probe may be a practical option for mass screening. These devices are less costly than standard ultrasound equipment, and their small size and mobility allow them to be used outside of hospitals for screening. This study assessed the effectiveness and reliability of such devices in finding and evaluating AAAs.

5.2 Summary of main findings

The objective of the first study was to estimate the AAA prevalence and associated risk factors in Riyadh and, it hypothesized that the prevalence of AAA in Riyadh is similar to that observed in Western countries and that a national screening program would be cost-effective. According to the findings, the prevalence (1%) of AAA in the examined sample is within the range of the last decade's reported prevalence in Western nations where AAA screening was implemented and economic (Song et al., 2023). The association between AAA and some risk factors was strong, with p-values of 0.002 and 0.001, respectively, for gender and smoking. Aortic diameter measurements obtained by conventional ultrasound had high intra-observer and inter-observer agreement, with ICC values greater than 0.86 and 0.9, respectively.

The second study's objective was to examine the elastic properties of both aneurysmal and non-aneurysmal aortic walls utilizing Shear Wave Elastography (SWE), and its hypothesis was that the wall of the aorta in aneurysms exhibits distinct elastic properties compared to non-aneurysmal aorta wall. The findings revealed a highly significant statistical difference in arterial wall stiffness between aneurysmal and non-aneurysmal walls ($p < 0.001$). Based on the interpretation of the findings, AAA walls are less stiff and more elastic. The third study's objective was to assess the reliability of the Butterfly iQ probe as a diagnostic tool for evaluating aortic aneurysms, and its hypothesis was that the efficacy of the Butterfly iQ probe

is comparable to that of a conventional ultrasound machine in evaluating AAA. The results found no systematic difference in aortic measurements acquired by the butterfly iQ probe or the conventional ultrasound machine, showing that neither probe consistently produced higher or lower measurements than the other. The Bland Altman limits widths were similar for both proximal and distal measurements, as well as between the two observers. The findings indicated that both the Conventional and Butterfly iQ machines had a high level of intra- and inter-observer agreement, with the majority of reported ICC values over 0.91.

5.3 The prevalence and risk factors associated with AAA in Riyadh, Saudi Arabia

5.3.1 AAA screening

In a sample of 680 people, AAA was found to be present in 1% (95% CI:0.4% - 2.1%) of the studied sample. This supports our initial hypothesis: the prevalence of abdominal aortic aneurysm (AAA) in Riyadh, Saudi Arabia, is comparable to that found in Western nations. According to recent studies, prevalence rates in developed countries have declined as a result of reduced tobacco use and better management of atherosclerotic disease (Earnshaw, J. J. & Lees, 2017).In the last two decades, reported prevalence varied from 1.1% in England to 1.5% in Sweden (Guirguis-Blake et al., 2014) (Carino et al., 2018)(Earnshaw, Jonothan J., 2018). The regional prevalence estimate in 2019 was 1.13% in Europe and 0.56% in America (Song et al., 2023).

Despite the fact that we found the same number of AAAs, the 1996 study by Al zaharni et al. conducted in Jeddah, western Saudi Arabia, reported a prevalence of 1.8% in the study sample (seven AAA cases) (Al Zahrani et al., 1996). This could indicate that their higher

reported prevalence is due to screening focusing on high-risk groups, such as those with peripheral vascular disease and hypertension, as research has shown that the risk of AAA development is significantly increased with the presence of such medical conditions. (Grøndal, Søgaard & Lindholt, 2015) (Jones et al., 2016) (Lindholt & Søgaard, 2017), another explanation could be the changing epidemiology of AAA globally, with a decline in the incidence of AAA over the past 20 years (Song et al., 2023). Existing literature attributed this decline to risk factor modification such as reduced tobacco consumption, better disease management and the introduction of endovascular aortic repair (EVAR) (Sampson et al, 2014). Given that Al zaharni et al. study was conducted more than 20 years ago and the prevalence of smoking among the adult population in Saudi Arabia has increased to 19.8% (Global Adult Tobacco Survey, 2019). In addition to our study being conducted solely by the investigator and exclusively involving participants visiting the ultrasound department on the designated data collection days, we suspect that the true population prevalence is much greater.

we are unable to offer a straightforward answer to whether a nationwide screening program would be cost-effective. In the United Kingdom, AAA screening is considered economically feasible if the prevalence is 1% or higher (Chabok et al., 2016). We cannot confirm that this is the case in Saudi Arabia due to a lack of information in that area, which requires further investigation: hospital capacity, allocated funding, rupture mortality rates, and screening costs. We addressed part of the question about prevalence, but because our study was limited to hospital attendees at four tertiary hospitals in Riyadh, Saudi Arabia's capital, and did not cover the entire country, we were unable to provide an answer for the acceptability nor participation rate as our study was limited to hospital attendees and participants were not invited for screening. We propose that a national screening program should be considered based on our findings. Since smoking is associated with a three to fourfold risk of AAA development, it is

thought that starting AAA screening in countries with high tobacco consumption is beneficial (Sprynger et al., 2019).

5.3.2 AAA risk factors

A significant correlation between gender and smoking status (both ever smoker and current smoker) and the incidence of AAA has been revealed in the correlation between a variety of risk factors and the existence of AAA (p-value 0.002 and 0.001, respectively). AAA was only detected in men; no females were reported to have the disease. AAA prevalence was considerably higher in current smokers (5.8% vs. 0.6% in nonsmokers), who had a significantly increased chance of developing the disease, given that smoking is associated with a 3 to 4-fold risk of AAA development (Sprynger et al., 2019). Smoking has been established as a significant risk factor for the formation and progression of aortic aneurysms. The toxic effects of smoking contribute to oxidative stress, which leads to a generalized vascular inflammation characterized by cytokine release, inflammatory cell adhesion, and, eventually, disruption of endothelial integrity and degradation of structural proteins in the aortic wall, increasing the susceptibility to aneurysm formation (Golbidi, Edvinsson & Laher, 2020).These findings are compatible with previous research that identified male gender and smoking as acknowledged risk factors for AAA(National Library, 2006) (Chaikof et al., 2009) (Altobelli et al., 2018).

Furthermore, there was some evidence of a possible relationship between a history of heart attacks and AAA, but this result was statistically insignificant (p=0.05). Those who have previously experienced a heart attack were shown to be more likely to develop AAA. AAA was discovered in just 0.7% of those who had never had a heart attack, compared to 3.5% of individuals who had a previous heart attack. The consensus from Previous studies have identified advanced age as a risk factor (Alcorn et al., 1996)) (Howell & Rabener, 2016) ,but

this was not the case in our study as the association between age, and the presence of AAA was not statistically significant (p-value 0.27). This could be because the age group recruited in our sample (> 50 years old) was younger than in previous studies where the cut-off age was 65 years old and all those examined were over 65.

Several studies have defined family history and PAD to increase the risk of developing AAA in patients (*AAA screening in SA is it worth it.* ; Xi Li et al., 2013) (Grøndal, Søgaard & Lindholt, 2015) (Eiman Jahangir et al., 2015); however, in our study, patients did not completely recognize the disease PAD or were ignorant that they had it; hence, their replies may not reflect the actual situation. PAD was reported in only 1.5% of the sample.

Diabetes was present in more than half of our individuals (50.9%), and prior research has linked diabetes to a lower risk of AAA. several studies have consistently supported the protective role of diabetes in reducing the aortic aneurysm growth. (Jahangir et al., 2015) (Carino et al., 2018) (Antonopoulos & Liapis, 2018)). According to the International Diabetes Federation (IDF), it was estimated that around 17.7% of the adult population in Saudi Arabia had diabetes in 2021 (IDF, 2021). This could have an impact on our predicted prevalence. Despite this, two of the detected AAAs were in diabetic patients, and one of them had a significantly calcified aortic wall (Figure 3.1).

Participants had high rates of hypertension and hyperlipidemia (58% and 65%, respectively), which is concerning for the overall health of the population because these are risk factors for several comorbidities such as cardiovascular disease and will consequently increase mortality rates and the burden on health services.In literature about AAA in women, hypertension has been identified as the primary risk factor for AAA, with a comparatively less impact in men.,

Hypertension was shown to be related with 93% of incidence acute AAA events in women, with a lower apparent effect in men. (Howard et al., 2015).

Aortic diameter measurements were reproducible with good intra-observer and inter-observer agreement where the ICCs values were greater than 0.86 and 0.9, respectively. This guarantees the dependability of our demonstrated results.

5.4 AAA Shear wave elastography (SWE) ultrasound

The result of this study supports our initial hypothesis. The identified statistically significant difference ($p < 0.001$) between arterial stiffness of aneurysmal aortic walls (mean 29 Kpa) and non-aneurysmal aortic walls (mean 70 Kpa), suggests that AAA walls are more elastic, which is consistent with the existing knowledge that AAA tend to develop with the weakening of the wall caused by a range of factors (Stather et al., 2014). These findings provide novel insights into the potential for predicting the risk of developing AAA by assessing the changes in aortic wall stiffness using SWE ultrasound. Consequently, this has the potential to enhance the practice of AAA detection and provide valuable diagnostic and monitoring information.

Diabetes, coronary artery disease (CAD), and excessive cholesterol were found to be strongly linked with AAA in the initial univariable analysis results (p-values 0.007, 0.002, and 0.02 respectively). A further multivariable analysis of the same factors, however, revealed that their association as independent risk factors was only of borderline statistical significance (p-values 0.08, 0.05, and 0.07, respectively), with the odds of AAA being more than three times higher for patients with diabetes or CAD than for patients without each factor. This was an unexpected finding given that most published research had diabetes as a protective factor against AAA; this will be explained further in a subsequent section on AAA and diabetes.

5.5 Butterfly iQ efficiency in AAA evaluation

5.5.1 Patient characteristics

This study sample (n=13) exhibited similar characteristics to the main study sample. The mean age of 73 years, with male predominance (85%). A quarter of the patients (23%) were current smokers, 46% were past smokers, and nearly one-third (31%) had never smoked. The average duration of smoking was 40 years. 69% of those who participated are hypertensive, and 54% have elevated cholesterol levels. Two of AAA cases were in female participants and three were in diabetics.

5.5.2 Probe comparison

It was reported in the Alfuraih et al study, which is considered the first-of-its-kind study comparing handheld ultrasound devices to conventional cart-based ultrasound in measuring the abdominal aorta that handheld devices are reliable for screening the abdominal aorta because intra- and inter-operator agreement was perfect, with all ICC values greater than 0.8. The inter-system ICCs were 0.81 for the proximal location and 0.87 for the distal location, in 91% of the cases, a 0.3 mm difference in values between machines was noted. One limitation of their study was the absence of AAA in their sample. (Alfuraih et al., 2021). This information was incorporated in our research, and our findings confirm the reliability and validity of handheld devices, specifically the Butterfly iQ probe, in large-scale AAA screening. Our findings paralleled theirs, with all intra- and inter-operator ICC values greater than 0.86 and 0.9, respectively. The intersystem comparison reported no systematic difference on average in

aortic measurements obtained by either the butterfly iQ probe or the conventional ultrasound machine, indicating that neither probe was consistently producing higher of lower measurements than the other with most reported ICC values exceeding 0.91 with <0.4 mm difference in pairs of measurements between machines in 85 % of the cases. The Bland Altman limits of agreement widths were similar for the conventional and butterfly methods, both proximal and distal measurements also for the two observers, suggesting a similar level of intersystem, intra-, and inter-operator agreement.

Despite the fact that the intersystem agreement intervals were slightly wider than the interobserver and intra-observer agreement intervals and the distal measurements for the Butterfly probe, observer 2 had lower measurements than observer 1 by a mean of around 0.16 cm. The width of the Bland Altman limits remains acceptable and indicates a nearly equivalent level of agreement.

5.6 AAA and diabetes

All three of our studies found AAA in diabetics, and the third study established a probable link between diabetes and AAA. The odds ratio is 3.64 (95% confidence interval: 0.85-15.6). This runs contrary to previously published research, in which Diabetes Mellitus is not recognized as a risk factor for AAA despite being a well-known risk factor for cardiovascular, cerebrovascular, and peripheral vascular diseases due to screening data showing that diabetics have a lower risk of developing the condition (AAA) and when present they demonstrated slower growth rate, lower rupture rate, decreased rate of mortality from AAA rupture (Lederle, F. A. et al, 2000) (Patel et al., 2018). Moreover, the southern community cohort study, USA (Jahangir et al., 2015) found an inverse relationship between diabetes mellitus and AAA. This paradoxical relationship has been explained by a number of aorta-protective mechanisms

linked to diabetes mellitus, such as hyperglycemia-mediated aortic stiffening, reduced aortic wall stress, decreased extracellular matrix (ECM) degradation, increased smooth muscle cell synthesis, and decreased levels of matrix metalloproteinases (Death et al., 2003) (Åstrand et al., 2007) (Golledge et al., 2008) (Antonopoulos & Liapis, 2018). These factors contribute to an aortic wall that is thicker and less likely to rupture. Furthermore, some clinical and experimental studies imply that diabetes mellitus medications might act as a preventative measure against the development of aneurysms (Patel et al., 2018). Some studies suggest that diabetic patients have a larger, denser, and more fibrotic aortic wall, which may account for their decreased risk of AAA (Åstrand et al., 2007) (Xiong et al., 2016) . Yet, because the correlation was demonstrated to be of borderline statistical significance, we cannot validate the link. It could be that AAA was prevalent among diabetic patients due to them exhibiting strong risk factors that contributed to its development such as smoking and hypertension. AAA was found in five Saudi diabetic patients, four of whom were male smokers with hypertension. The diabetic female patient had a high BMI, elevated cholesterol levels, and hypertension, which might be explained with the fact that hypertension is considered the major risk factor for AAA in women. (Howard et al., 2015)

5.7 Healthcare in Saudi Arabia

5.7.1 Health care system

The healthcare sector in Saudi Arabia has witnessed significant advancements and improvements in recent years. The Saudi Arabian government has made substantial investments in the healthcare sector, resulting in the development of advanced infrastructure,

state-of-the-art medical facilities, and a highly proficient workforce. The privatization of the healthcare industry has been highlighted in Saudi Arabia's Vision 2030 (Rahman, 2020). The country offers a diverse array of services to its population and residents in which access to healthcare is guaranteed through a blend of public and private healthcare organizations, with primary healthcare clinics serving as the initial point of contact for the majority of individuals. In addition, Saudi Arabia has enforced a compulsory health insurance system, which enhances the affordability and availability of medical treatments. Furthermore, it places importance on proactive healthcare measures, including vaccinations and health education initiatives (Al-Hanawi, Khan & Al-Borie, 2019; Alkhamis, 2012). National screening for abdominal aortic aneurysm (AAA) has not yet been established in Saudi Arabia and adjacent countries such as the United Arab Emirates, Qatar, Egypt, and Jordan. There is a scarcity of research and little knowledge on AAA in the Middle East (Janho et al., 2019). Similarly, in Turkey, there is currently no such screening program. However, a study was conducted to evaluate the use of transthoracic echocardiography for screening AAA. The study found a relatively high prevalence of 2.93% of unknown AAA among a sample of 1948 individuals (Nair et al., 2019).

5.7.2 Potential challenges

It is important to take into account many potential challenges that may arise during the establishment of a nationwide screening program for Abdominal Aortic aneurysm (AAA). The absence of widespread public knowledge and comprehension about AAA, the factors that contribute to its occurrence, and the significance of undergoing screening might be a notable challenge. The availability and reach of screening facilities may provide difficulty, particularly in distant or underprivileged regions. Setting up and maintaining the required infrastructure for

AAA screening, which includes ultrasound technology and skilled staff, might pose a logistical challenge. It is essential to allocate adequate financing and resources to facilitate the establishment and long-term viability of a nationwide AAA screening program. Obtaining financial support from the government, healthcare institutions, or other funding sources might be an obstacle. integrating the AAA screening program into preexisting healthcare processes and guidelines could be complicated. The process of creating and carrying out national policies, as well as ensuring that the program is in line with current healthcare regulations and securing the required approvals, might present difficulties. It is vital to establish a strong data management system in order to gather, evaluate, and safeguard patient data. Ensuring compliance with privacy standards and resolving issues about data security and confidentiality may present challenges as well. Finding an abdominal aortic aneurysm through screening may need adequate follow-up and treatment. Ensuring the presence of specialist facilities and resources for the handling of recognized patients might be a difficulty, especially in areas with restricted healthcare infrastructure. Securing the support and dedication of crucial stakeholders, such as healthcare managers, decision-makers, and medical professionals, could need the use of efficient engagement strategies. Establishing agreements, resolving issues, and promoting cooperation among diverse parties can be difficult. To tackle these challenges, it will be necessary to engage in precise strategic planning, encourage teamwork, and advocate for the successful implementation of a nationwide AAA screening program.

Conclusion

6.1 Conclusion

In conclusion, the data in this thesis demonstrated that the prevalence of AAA among Riyadh residents has been trending in line with that of Western nations in the past decade and that the idea of nationwide screening for AAA should be seriously considered and investigated. In addition to the benefit of improving patient survival rates, screening will provide substantial financial advantages when the prevalence of AAA is equal to or greater than 1%. Advances in ultrasound technologies have increased the capability of surveillance programs by enabling the incorporation of new predictors. Changes in the elasticity of the aortic wall may act as an early warning sign of AAA. The ongoing downsizing of scanning devices continues to facilitate and improve population surveillance programs. Our findings give credibility to the effectiveness of handheld portable devices, and more specifically the Butterfly iQ probe, in the detection and evaluation of AAA, implying that it could possibly serve as a substitute for conventional ultrasound machines in community mass screenings that are not necessarily performed in hospitals.

6.2 Limitations

The findings presented in this study should be viewed in light of several potential limitations. The first restriction is related to the study design, as the screening was not conducted in the community but rather in a hospital setting in Riyadh, with only patients attending hospitals for appointments being screened. As a result, neither the acceptability nor participation rate nor the cost or exact prevalence among the Saudi people can be determined. The second limitation is that our study included both male and female participants. In contrast to prior research on the topic and current national screening programs which have primarily focused on screening male participants for AAA. it is important

to acknowledge that the exclusion of women from the initial sample size of 680, could potentially lead to an increased prevalence of aneurysm disease (2.4%) compared to previous estimates of prevalence (1%). additionally, our study deviated from current screening programs, which typically targeted individuals aged 65 years or older. In contrast, participants aged 50 years and older were included in our study. Therefore, it is worth exploring the impact of raising the age threshold for screening from 50 to 60 years, as such an adjustment could have further implications on the observed prevalence rates. Further emphasizing the importance of gender and age criteria in the screening process. The third limitation is that, due to the small number of AAA cases in the prevalence study, multivariable analysis to explore the independent association between AAA and risk factors was not possible since mathematical issues could arise where the odds ratio cannot be calculated in certain groups that have no occurrences of AAA, such as the absence of AAA in female patients and those who never smoked. More simply, when there are too many variables with too little data, the models' supporting algorithms fail to converge. That is, we may not obtain any results at all at times, or we may get untrustworthy results. Finally, due to the expiration of ethical approvals and time constraints in carrying out the study, the Butterfly iQ study was limited to patients with AAA at one hospital (NGHA), resulting in a smaller sample size.

6.3 Practical implications

6.3.1 Patient recruitment enhancement

Enhancing the recruitment of patients for AAA screening can be accomplished through many approaches: first, by initiating specific awareness efforts to educate the public about AAA, its risk factors, and the significance of screening using several media platforms, such TV, radio, social media, and community activities to efficiently reach a large number of people and urge them to take part in screening campaigns. Second, by Involving primary care clinicians, such

as general practitioners and family doctors, to identify individuals who are appropriate for AAA screening and refer them to screening. Teaching healthcare workers about the advantages of screening along with providing them with screening protocols and tools can improve patient recruitment. In addition, creating referral channels and promoting collaboration between primary care doctors and screening facilities can simplify the process and help patients sign up. Third, identifying and focusing on high-risk populations, such as older adults, smokers, and those with a family history of AAA, can improve patient recruitment. Working together with certain community groups where there is a higher occurrence of risk factors can aid in efficiently reaching the target population. In addition to improving the screening process by reducing administrative obstacles, simplifying registration procedures, and assuring efficient appointment scheduling. Providing benefits, such as lower-priced or complimentary screening, might encourage patients to take part in screening. Finally, Collaboration in Research and Partnerships between the Public and Private Sectors: Working together with research institutes, healthcare organizations, and relevant stakeholders may utilize their resources, skills, and networks to enhance patient recruitment. Collaborations between the public and commercial sectors can also help with focused communication, the pooling of resources, and the use of creative methods to attract patients.

6.3.2 Clinical impact

To engage healthcare authorities and establish a nationwide screening program for Abdominal Aortic Aneurysm (AAA) in Saudi Arabia, the following measures should be considered: Initially, emphasizing the significance of early detection and possible advantages to the population of Saudi Arabia, including reduced fatality rates and medical costs. furthermore, identifying key stakeholders who have the authority and influence to make decisions regarding

healthcare policies and programs in Saudi Arabia and crafting a clear and compelling message that emphasizes the importance of AAA screening and its potential impact on public health. This may involve government officials, policymakers, healthcare administrators, and representatives from relevant medical societies. Additionally, reaching out to healthcare professionals, including physicians, surgeons, and specialists, who can provide expert opinions and advocate for the implementation of a national AAA screening program as their support and endorsement can carry significant weight in influencing health leaders. Conducting awareness campaigns to Raise public awareness about AAA, its risk factors, and the importance of early detection. to encourage individuals to seek screening services. Finally, collaborating with relevant organizations, such as patient advocacy groups, medical societies, and research institutions, and working closely with policymakers and health leaders to advocate for the integration of AAA screening into national healthcare policies and guidelines. Providing them with evidence, expert opinions, and success stories from other countries that have implemented similar programs.

6.4 Further research recommendations

This research has raised many questions that need to be further investigated prior to the implementation of AAA screening in Saudi Arabia. A further study on the prevalence of AAA among the Saudi general population or community from cities all over the kingdom of Saudi Arabia, not in a hospital-based setting is recommended to determine the exact prevalence, high-risk groups, and the necessity of national screening program or whether screening should be more targeted to high-risk groups. It is recommended that additional research be conducted to validate the cost-effectiveness of screening in Saudi Arabia given that it is affected by several potential challenges, such as the budget allocated for health services and the support from

government authorities, the capacity of the healthcare system to handle many screenings, and the lack of awareness and understanding of the importance of AAA screening among the general population and healthcare providers. This could result in low participation rates and poor uptake of the program. It would be beneficial to examine the long-term change in aortic wall elasticity in sub-aneurysmal aortas and small AAAs using SWE ultrasound to gain a better understanding of the disease progression. There is abundant room for additional research with an emphasis on the differences in image quality between handheld devices and conventional ultrasound in evaluating the aorta.

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Appendices

Appendix.1: Ethical approval (PNU):

Kingdom of Saudi Arabia
Ministry of Education
Princess Nourah Bint Abdulrahman University
(048)

المملكة العربية السعودية
وزارة التعليم
جامعة الأميرة نورة بنت عبدالرحمن
(٠٤٨)

Institutional Review Board — مجلس المراجعة المؤسسي

IRB Registration Number with KACST, KSA: H-01-R-059

October 6, 2019
IRB Log Number: 19-0171
Project title: The prevalence Abdominal Aortic Aneurysm (AAA): An Ultrasound screening program for the aging population in multicentre across Riyadh
Category of Approval: EXPEDITED

Dear Arwa Algadi,

Thank you for submitting your proposal to the PNU Institutional Review Board. Your proposal was evaluated considering the national regulations that govern the protection of human subjects. The IRB has determined that your proposed project poses minimal risk to the participants. Therefore, your proposal has been deemed ***EXPEDITED*** from IRB review. Please note that this approval is from the research ethics perspective only. You will still need to get permission from the head of the department in PNU or an external institution to commence data collection.

Please remove from the questionnaire the following personally identifying information: name, medical record number, mobile number, date of birth, and signature. You can use a study number on each questionnaire to link to such information that will be kept under lock in a safe place.

Please be informed that in conducting this study, you as the Principal Investigator are required to abide by the rules and regulations of the Government of Saudi Arabia, the PNU/IRB policies and procedures, and the ICH Good Clinical Practice guidelines. You also need to notify the IRB as soon as possible in the case of any amendments to the project, termination of the study, any serious unexpected adverse events, or any event or new information that may affect the benefit/risk ratio of the proposal. For any proposed changes in your research protocol, please submit a Request for Modification form to the PNU IRB. Please be aware that changes to the research protocol may prevent the research from qualifying for expedited review and require submission of a new IRB application or other materials to the PNU IRB.

Please be advised that regulations require that you submit a progress report on your research every 6 months. Please refer to the protocol number denoted above in all communication or correspondence related to your application and this approval. You are also required to submit any manuscript resulting from this research for approval by IRB before submission to journals for publication.

We wish you well as you proceed with the study. Should you have additional questions or require clarification of the contents of this letter, please contact me.

Sincerely Yours,

[redacted]

Prof. Omar H. Kasule Sr.
Chairman, Institutional Review Board (IRB)
Princess Nourah bin Abdulrahman University, Riyadh, KSA
Tel: +966 548867916
E-mail: irb@pnu.edu.sa

جامعة الأميرة نورة بنت عبدالرحمن
مجلس المراجعة المؤسسي
Institutional Review Board (IRB)
06 OCT 2019

الرقم : التاريخ : / / 143هـ المشفوعات:

Appendix.2: Ethical approval (KSMC):

Kingdom of Saudi Arabia
Ministry of Health
King Saud Medical City

مدينة الملك سعود الطبية
KING SAUD MEDICAL CITY

المـملكة العـربية السـعوديـة
وزارة الـصحة
مدينة الملك سـعود الطبية

INSTITUTIONAL REVIEW BOARD (IRB)
***IRB Registration Number with KACST, KSA*: H-01-R-053**

- Memorandum -

Date: August 18, 2020

Project Reference No.	: **H1RE-24-Dec19-03**
Proposal Title	: "The prevalence Abdominal Aortic Aneurysm (AAA) : an Ultrasound Screening program for the aging population in multicentre across Riyadh"
PI	: Ms. Arwa Algadi
Co-Investigators	: Mazen Mohammed Abounassif
Category of Approval	: Continuing Review
Date of IRB Approval-Expiration (Validity)	: 18/08/2020 to 17/02/2021 (6 months)

Dear Ms. Arwa Algadi:

We are pleased to inform you that the above-referenced research proposal has been reviewed and was approved, as continuing review. To continue the collection of data a permission letter must be issued from the Director of the Research Center first.

This approval is valid for 6 months from the date of IRB review when approval is granted. The approval will no longer be in effect on the date listed above as the IRB expiration date. Please note that you are obligated to submit the following to IRB committee:

1. progress/final report on the 6months (17-Feb-2021) (or earlier in the case the study has completed)
2. any manuscript resulting from this research for approval by IRB before submission to journals for publication.

The approval of the conduct of this proposal will be automatically suspended after 06 months, in the case the Progress Report (or Final Report, if relevant) is pending acceptance. You also need to notify the Research Centre as soon as possible in case of:

1. any amendments to the proposal;
2. termination of the study;
3. any serious or unexpected adverse events;
4. any event or new information that may affect the benefit/risk ratio of the proposal.

All records relating to the research including consent form must be retained and available for audit for at least 3 years after the research has ended.

We wish you every success in your research endeavors.

[redacted]

Chairman, Institutional Review Board (IRB)
King Saud Medical City Riyadh, KSA

وزارة الصحة المملكة العربية السعودية
مدينة الملك سعود الطبية
King Saud Medical City
(IRB) لجنة أخلاقيات البحوث

☎435-5555 Ext. 2345 irb@ksmc.med.sa

Appendix.3: Ethical approval (KKUH):

Kingdom of Saudi Arabia
King Saudi University (034)
P.O. Box 7805 Riyadh 11472
Tel: +966 11 467 00 11
Fax: +96611 467 19 92
http://medicalcity.ksu.edu.sa

المملكة العربية السعودية
جامعة الملك سعود (٣٤)
ص.ب ٧٨٠٥ الرياض ١١٤٧٢
هاتف: +٩٦٦١١٤٦٧٠٠١١
فاكس: +٩٦٦١١٤٦٧١٩٩٢

جامعة الملك سعود
King Saud University
المدينة الطبية الجامعية

08.03.2020 (13.07.1441)
Ref. No. 20/0156/IRB

To: **Dr. Nasser Alkamees**
Director of King Fahad Cardiac Centre
Head of Surgery Division
King Saud University Medical City
Email: naalkhamees@ksu.edu.sa
Principal Investigator

Cc: Arwa Algadi – arwa.algadi@gmail.com
Co-investigator

Subject: **IRB Approval on Research Project No. E-20-4550**
Study Title: "The Prevalence of Abdominal Aortic Aneurysm (AAA): An Ultrasound Screening Program for the Aging Population in Multicenter Across Riyadh"
Type of Review: Full-Board
Date of Approval: 04 March 2020
Date of Expiry: 04 March 2021

Dear Dr. Nasser Alkamees,

Thank you for your response to the comments of the Board regarding the above-mentioned research project which was reviewed and discussed in the IRB Meeting 05 (Academic Year 1440-1441) held on 30 January 2020 (05 Jumaada-II 1441). The revised proposal submitted in response to the comments of the board and the clarifications provided are satisfactory. Therefore, the project is now **approved**. You are granted permission to conduct this study as approved by the IRB.

Please be informed that in conducting this study, you as the principal investigator, are required to abide by the rules and regulations of the Government of Saudi Arabia, the KSUMC IRB policies and procedures and the ICH-GCP Guidelines. This approval shall remain valid until the expiry date noted above assuming timely and acceptable responses from the IRB's periodic requests for surveillance and monitoring information, with the following terms and conditions:

1. **Modifications to Research/ Amendments to the approved project:** any modifications to the research (including changes to the informed consent document(s) must receive IRB approval prior to implementation of the changes. Substantial variations may require new submission.
2. **Annual Reports:** continued approval of this project is dependent on the submission of annual reports. If you wish to have your protocol approved for continuation, please submit a completed **request for reapproval of an approved protocol form (KSU-IRB 017E) at least 30 days before the expiry date**. Failure to receive approval for continuation before the expiration date will result in automatic suspension of the approval of this protocol on the expiration date. Information collected following suspension is unapproved research and can never be reported or published as research data.
3. All unforeseen events that might affect continued ethical acceptability of the project should be reported to the IRB as soon as possible.
4. Any serious unexpected adverse events should be reported within 48 hours (2 days).

Appendix.4: Ethical approval (NGHA):

Kingdom of Saudi Arabia
Ministry of National Guard - Health Affairs

المملكة العربية السعودية
وزارة الحرس الوطني - الشؤون الصحية

King Abdullah International Medical Research Center
(KAIMRC)

IRB NCBE Registration No.: H-01-R-005

(84) 94456 1515 94466 irb@ngha.med.sa

IRB Office Memo Ref.No. IRBC/1157/20 E-CTS Ref. No. RYD-20-419812-60277

Study Number: **SP20/088/R**
Study Title: **The prevalence of Abdominal Aortic Aneurysm (AAA): an ultrasound screening program for the aging population in multicenter across Riyadh**
Study Sponsor: **Non grant**
IRB Approval Date: **13 July 2020**
IRB Review Type: ■ **Expedited Review** ☐ **Full Board**
Study site(s): **Central Region**

Dear **Dr. Ali Aldhebaib**
Assistant Professor, Radiological Sciences, KSAU-HS
Ministry of National Guard – Health Affair

Sub-investigator: Arwa Algadi

After reviewing your submitted research proposal/protocol and related documents, the **IRB has APPROVED** the submission. The approval includes the following related documents:

Document/Title	Version	Date
Research Proposal	01	13 July 2020
Data Collection Form	01	13 July 2020
Inform Consent Form	01	13 July 2020

The approval of the research study is valid for **one year** from the above approval to expiration date.

Terms of Approval:

- **Annual Reports:** An Annual report must be submitted for approval to avoid termination/suspension of your research.
- **Financial report:** If your study is funded project, details financial report should be submitted with the scientific report.
- **Final Report:** After completion of the study, a final report must be forwarded to the IRB.
- **Retention of original data:** The PI is responsible for the storage and retention of original data pertaining to the project for a minimum of five years.
- **Reporting of adverse events or unanticipated problems:** The PI is responsible to report any serious or unexpected adverse events or unanticipated problems, which could involve any risk to participants or others, or any event on incidents that may have impact on the research or participants.
- **Biological samples:** No biological samples to be shipped out of the Kingdom of Saudi Arabia without prior IRB approval.
- **Participant incentives:** No financial compensation or gifts to be given to participants without prior IRB approval.
- **Storage of biological samples:** All biological samples collected for the purpose of this research must be stored in the KAIMRC related repository.
- You will need to resubmit the proposal to the IRB for review and re-approval before implementing any changes to the approved proposal.
- It is possible that the IRB may decide that the proposed new changes may exclude the proposal from being accepted for exempt review.
- It is your responsibility to safely store the data collected.
- Please note that phone based surveys are not permitted.
- If your approved proposal requires access to Bestcare, please write to the IRB informing them of the name of the designated data collector and exactly define the period requested for collecting data. Do not start the data collection until an approval memo is issued from the IRB giving permission to that collector to start accessing Bestcare for the duration of the project and after signing a confidentiality agreement.

[redacted] 25 AUG 2020

Prof. Abdullah Al Sayyari
Chairman, Institutional Review Board (IRB)
Ministry of National Guard - Health Affairs

AS/HK/FAS

[redacted]

P.O. Box 22490, Riyadh 11426
Tel. 8011111
Telex : 403450 NGRMED SJ
(ORACLE 29795)
HA . Printing Press 17 / 137

ص.ب. ٢٢٤٩٠ الرياض ١١٤٢٦
تلفون ٨٠١١١١١
تلكس ٤٠٣٤٥٠

Appendix.5: PNU patient consent form (Arabic language):

Form IRB-10.10.01

Minimal Risk Informed Consent Template

إقرار بالموافقة المستنيرة على المشاركة في بحث علمي يشتمل علي الحد الأدنى من المخاطر

Effective Date: 6/10/2019 PNU Institutional Review Board

رقم البحث العلمي	19-0171
اسم المشارك	
رقم السجل الطبي	
عنوان البحث العلمي	**مدى انتشار التوسع في الشريان الأورطي البطني في السعودية، فحص باستخدام الموجات الفوق صوتية للمتقدمين بالعمر في مستشفيات مدينة الرياض**
الباحث الرئيس	أروى القاضي
العنوان	قسم العلوم الإشعاعية كلية الصحة و علوم التأهيل جامعة الأميرة نورة بنت عبدالرحمن مكتب ٣٠٣٠٥
رقم الهاتف	٠١١٨٢٤٠٧٤٠

ما سبب القيام بهذا البحث العلمي؟

لمعرفة مدى انتشارالتوسع في الشريان الأورطي البطني و تشخيصه مبكراً و تفادي المضاعفات الممكن حصولها.

كم عدد الأشخاص المفترض مشاركتهم في هذا البحث العلمي؟

٦٨٠ شخص

ماذا يتضمن هذا البحث العلمي؟

موقع إجراء هذا البحث العلمي: عدد من مستشفيات مدينة الرياض

ما المطلوب مني خلال هذا البحث العلمي؟

منحنا ١٠ دقائق من وقتك لإتمام الاستبيان و أخذ بعض القياسات للأورطي بعد الانتهاء من فحص الموجات الفوق صوتية الخاص بك.

كم مدة مشاركتي في هذا البحث العلمي؟

١٠ دقائق

هل يمكنني إنهاء المشاركة في هذا البحث العلمي؟

المشاركة طوعيه محضة ويمكنك أن تنهيها في أي وقت تشاء.

ما هي فوائد هذا البحث العلمي؟

تشخيص توسع الشريان الأورطي البطني مبكراً في حال تواجده و التمكن من اتخاذ الإجراء اللازم و تفادي المضاعفات.

ما هي المخاطر المتوقعة من المشاركة في هذا البحث العلمي؟

لا يوجد أي خطر من مشاركتك.

ماذا سيحدث إذا أصابني ضرر جراء المشاركة هذا البحث العلمي؟

إذا حدث أن أصبت بضرر نتيجة مشاركتك في هذا البحث العلمي، سيقدم لك مستشفى الملك عبد الله الجامعي العلاج دون أي تكلفة لك.

وما هي تكاليف المشاركة في هذا البحث العلمي؟

لا توجد تكاليف للمشاركة في هذه هذا البحث العلمي.

هل هنالك اجر مقابل المشاركة في هذا البحث العلمي؟

لا يوجد أجر.

ما هي البدائل؟

لا يوجد بدائل.

هل سيتم الحفاظ على معلوماتي بسرية؟

معلوماتك الشخصية سيتم الحفاظ عليها بسرية تامة. ولا تعطي إلا إذا اقتضى الأمر وذلك في حدود النظم والقوانين المطبقة بهذا الخصوص. معلوماتك الشخصية لن تستخدم في أي تقارير.

ما هي حقوقي إذا شاركت في هذا البحث العلمي؟

المشاركة في هذا البحث العلمي هي بمحض اختيارك. يمكنك أن تختار المشاركة أو لا. إذا قررت أن تشارك في هذا البحث العلمي، يمكنك التوقف في أي وقت تشاء. وإذا لم تشارك لن تكون هناك أي عقوبة لك, ولا تتأثر الرعاية الطبية المقدمة لك بسبب هذا القرار.

Form IRB-10.10.01

Minimal Risk Informed Consent Template

إقرار بالموافقة المستنيرة على المشاركة في بحث علمي يشتمل علي الحد الأدنى من المخاطر

Effective Date: 6/10/2019 PNU Institutional Review Board

بمن يمكنني الاتصال إذا كان لدي أسئلة أو مشاكل؟

إذا كانت لديك أسئلة عن هذا البحث العلمي، يمكنك الاتصال بالباحث الرئيس على هذا الرقم ٠(١١)٨٢٤٠٧٤٠. إذا كانت لديك أي تساؤلات حول "حقوق الاشخاص موضوع البحث، "يمكنك الاتصال برئيس لجنة أخلاقيات البحث العلمي (IRB) على الرقم ٠٠٩٦٦٥٤٨٨٦٧٩١٦ .

إقرار بالموافقة

المشارك

أقر أنا بأن هذا البحث العلمي وإجراءاته قد تم شرحها لي. لقد سمح لي بأن اسأل كل سؤال لدي الآن. ويمكنني أن اسأل أي أسئلة إضافية في أي وقت لاحق. كما يمكنني إنهاء المشاركة في هذا البحث العلمي في أي وقت دون أن تتأثر الرعاية الصحية المقدمة لي.
سأحصل على نسخة موقعة من الإقرار بالموافقة.

توقيع المشارك: _____

التاريخ / /

الوقت (ص ☐ م☐)

الشخص الحاصل علي الإقرار بالموافقة

أقر بأنني قد شرحت بصورة كاملة, طبيعة هذا البحث العلمي والغرض منه وما ينطوي عليه من مخاطر. ولقد أجبت على جميع الأسئلة بقدر الإمكان. سأعطي نسخة موقعة من الإقرار بالموافقة للمشارك المذكور أعلاه.

توقيع الشخص الحاصل علي الإقرار بالموافقة : _____

التاريخ: / /

الوقت ص ☐ م☐

الباحث الرئيس

توقيع الباحث الرئيس _____

الوقت ص ☐ م☐

Appendix.6: data collection sheet in Redcap:

patinet consent

Please complete the survey below.

Thank you!

please find the attached informed patient consent form

[Attachment: " patient consent form.pdf"]

please upload patient consent form

Patient Data

first name	_____
last name	_____
Hospital	◯ KAAUH ◯ KSMC ◯ NGHA ◯ KKUH ◯ KFMC
Department	◯ general ultrasound ◯ echocardiography ◯ vascular ultrasound ◯ outpatient clinic ◯ other
specify	_____
Medical record number	_____
Date of birth	_____
age	_____

Tests results

Electrocardiogram (ECG) result	◯ normal ◯ abnormal ◯ not availabe
diagnosis and comments	_____
Blood pressure (systolic/diastolic)	_____
BP reading within normal	◯ yes ◯ no
comment	_____

Ultrasound measurments

suprarenal aorta diameter (cm) _____

Infrarenal aorta diameter (cm) _____

above bifurcation Aorta diameter (cm) _____

Right iliac artery diameter (cm) _____

Left Iliac artery diameter (cm) _____

does the patient has AAA
◯ yes
◯ no
◯ not clear by U/S

IMT = _____

comments _____

lipid profile blood test

* Total Cholestrol _____

unit
◯ mmol/L
◯ mg/dL

within normal range
◯ yes
◯ no
(refrence rage =0.13 - 5.18 mmol/L)

* HDL cholestrol _____

unit
◯ mmol/L
◯ mg/dL

within normal range
◯ yes
◯ no
(reference range =>1.55 mmol/L)

* LDL cholesterol _____

unit
◯ mmol/L
◯ mg/dL

within normal range
◯ yes
◯ no
(reference range =< 2.59 mmol/L)

* Triglycerides _____

unit
◯ mmol/L
◯ mg/dL

within normal range
◯ yes
◯ no
(refrence range =< 1.69 mmol/L)

sugar blood test

*Hemoglobin A1C (%) _____

within normal range
◯ yes
◯ no
(reference range =4.4 - 6.4 %)

* Fasting blood glucose _____

unit
◯ mmol/L
◯ mg/dL

within normal range
◯ yes
◯ no
(refrence range =4.6 - 6.4 mmol/L)

* Random blood glucose _____

unit
◯ mmol/L
◯ mg/dL

within normal range
◯ yes
◯ no
(reference range= 2.9 - 7.8)

*glucose tolerance test _____

unit
◯ mmol/L
◯ mg/dL

within normal range
◯ yes
◯ no

Basic metabolic and Renal function profile blood tests

* sodium (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range=136 - 144 mmol/L)

* potassium (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range= 3.6 - 5.1 mmol/L)

* total CO2 (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range =22 - 32 mmol/L)

* chloride (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range = 101 - 111 mmol/L)

* Albumin (g/L) _____

within normal range
◯ yes
◯ no
(refrence range=35 - 48 g/L)

* Calcium (mmol/L) _____

within normal range
◯ yes
◯ no
(refrenece range= 2.23 - 2.58 mmol/L)

* creatinine (umol/L) _____

unit
◯ umol/L
◯ mmol/L

within normal range
◯ yes
◯ no
(refrence range= 54 - 110 umol/L)

* Magnesium (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range = 0.74 - 1.03 mmol/L)

* Phosphours (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range= 0.81 - 1.49 mmol/L)

* Uric Acid (Urate) (umol/L) _____

within normal range
◯ yes
◯ no
(refrence range= 286 - 518 umol/L)

* urea (BUN) (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range= 2.9 - 9.3 mmol/L)

* Corr Calcium (mmol/L) _____

within normal range
◯ yes
◯ no
(refrence range= 2.23 - 2.58 mmol/L)

* Albumin (g/L)	_____
within normal range	◯ yes ◯ no (refrence range=35 - 48 g/L)
* Calcium (mmol/L)	_____
within normal range	◯ yes ◯ no (refrenece range= 2.23 - 2.58 mmol/L)
* creatinine (umol/L)	_____
unit	◯ umol/L ◯ mmol/L
within normal range	◯ yes ◯ no (refrence range= 54 - 110 umol/L)
* Magnesium (mmol/L)	_____
within normal range	◯ yes ◯ no (refrence range = 0.74 - 1.03 mmol/L)
* Phosphours (mmol/L)	_____
within normal range	◯ yes ◯ no (refrence range= 0.81 - 1.49 mmol/L)
* Uric Acid (Urate) (umol/L)	_____
within normal range	◯ yes ◯ no (refrence range= 286 - 518 umol/L)
* urea (BUN) (mmol/L)	_____
within normal range	◯ yes ◯ no (refrence range= 2.9 - 9.3 mmol/L)
* Corr Calcium (mmol/L)	_____
within normal range	◯ yes ◯ no (refrence range= 2.23 - 2.58 mmol/L)

Appendix.7: SWE data collection sheets in Redcap:

SWE AAA

Record ID	_____
Gender	☐ male ☐ female
age	_____
weight	_____
height	_____
BMI	_____
DM	◯ Yes ◯ No
HTN	◯ Yes ◯ No
High cholesterol	◯ Yes ◯ No
CAD	◯ Yes ◯ No
Smoker	◯ Yes ◯ No
AAA AP diameter	_____
SWE measurement	_____
image 1	
image 2	
image 3	
image 4	
image 5	

SWE AAA

Record ID	_____
Gender	☐ male ☐ female
age	_____
weight	_____
height	_____
BMI	_____
DM	◯ Yes ◯ No
HTN	◯ Yes ◯ No
High cholesterol	◯ Yes ◯ No
CAD	◯ Yes ◯ No
Smoker	◯ Yes ◯ No
AAA AP diameter	_____
SWE measurement	_____
image 1	
image 2	
image 3	
image 4	
image 5	

Appendix.8: IQ butterfly Vs. Philips data collection sheets in Redcap:

participant's demographics

Record ID	_____
first name	_____
last name	_____
gender	◯ Male ◯ Female
age	_____
MRN	_____
Wieght	_____ (kg)
Height	_____ (cm)
Smoking	◯ Yes ◯ No
current smoker	◯ Yes ◯ No
how long have you been smoking?	_____
rate of smoking	_____
Diabetes M	◯ Yes ◯ No
Hypertension	◯ Yes ◯ No
High cholesterol	◯ Yes ◯ No

Conventional U/S

Image 1

Image 2

Image 3

Image 4

Image 5

Image 6

Image 7

Image 8

Operator 1

proximal measurement 1 _____

proximal measurement 2 _____

proximal measurement 3 _____

Distal measurement 1 _____

Distal measurement 2 _____

Distal measurement 3 _____

OTO measurement _____

Operator 2

proximal measurement 1 _____

proximal measurement 2 _____

proximal measurement 3 _____

Distal measurement 1 _____

Distal measurement 2 _____

distal measurement 3 _____

oto measurement _____

Butterfly IQ U/S

Image 1

Image 2

Image 3

Image 4

Image 5

Image 6

Image 7

Image 8

Operator 1

proximal measurement 1 _____

proximal measurement 2 _____

proximal measurement 3 _____

Distal measurement 1 _____

Distal measurement 2 _____

Distal measurement 3 _____

OTO measurement _____

Operator 2

proximal measurement 1 _____

proximal measurement 2 _____

proximal measurement 3 _____

Distal measurement 1 _____

Distal measurement 2 _____

Distal measurement 3 _____

OTO measurement _____